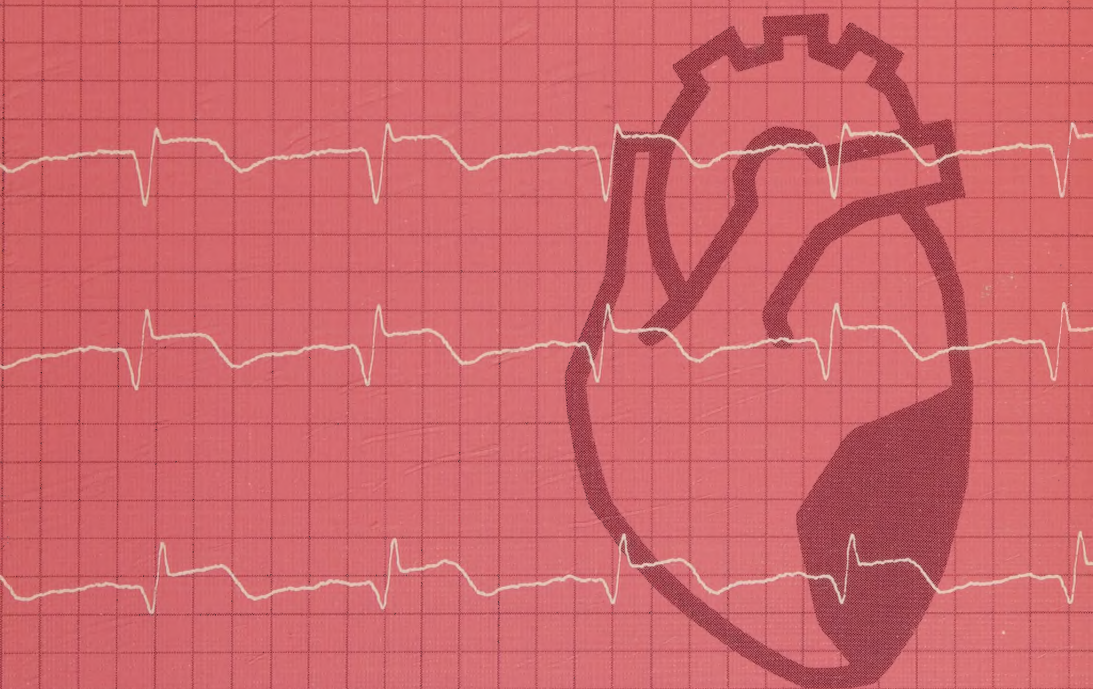


KRISTIAN THYGESEN

Assessing acute
myocardial infarction
by electro-
cardiography



ODENSE UNIVERSITY PRESS 1981

Forsvaret finder sted fredag den 4. dec. 1981 kl. 14.00
i patologisk instituts store auditorium, Odense sygehus.

Officielle opponenter: Peter R. Maroko og Torben Haghfelt

Assessing acute myocardial infarction by electro- cardiography

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Denmark



ODENSE UNIVERSITY PRESS · 1981

Denne afhandling er den 3. novbr. 1981 af det lægevidenskabelige fakultet ved Odense universitet antaget til for-
svar for den medicinske doktorgrad.

Jørgen Ringsted
h.a.dec.



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Tryk: OAB-Tryk, Odense
ISBN 87 7492 357 9

The present survey is based upon the following articles:

- I: Thygesen, K., Hørder, M., Nielsen, B.L. & Petersen, P.H.: The variability of ST segment in the early phase of acute myocardial infarction. Acta Med Scand (Suppl)623:61, 1979.
- II: Thygesen, K., Hørder, M., Nielsen, B.L. & Petersen, P.H.: Evolution of ST segment and Q and R waves during early phase of inferior myocardial infarction. Acta Med Scand 205:25, 1979.
- III: Thygesen, K., Hørder, M., Petersen, P.H. & Nielsen, B.L.: Praecordial ECG-mapping in acute anterior myocardial infarction: the variability of ST segment, Q and R waves. Scand J Clin Lab Invest 40:371, 1980.
- IV: Thygesen, K., Hørder, M., Petersen, P.H. & Nielsen, B.L.: Praecordial ECG mapping in acute anterior myocardial infarction. The evolution of ST segment and Q and R waves. Acta Med Scand 209:161, 1981.

The articles are referred to in the text by their Roman numbers.



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PREFACE

The present study was carried out in 1976-79 at the Medical Department B of the Odense University Hospital, during my appointment as a research fellow, first under the auspices of the Danish Heart Foundation and later Odense University.

I am extremely grateful to Bent Lyager Nielsen, M.D. who aroused my interest in the idea upon which the work is based and who guided me throughout the investigation. He was also instrumental in ensuring that I received financial support and excellent working conditions.

The investigation gave rise to the continuing close cooperation with Professor Mogens Hørder, M.D. for which I wish to express my appreciation. His scientific acumen has been of immeasurable help in completing the study.

I am greatly indebted to Per Hyltoft Petersen, M.Sc. whose profound knowledge of the natural sciences and statistics has been invaluable.

The advice and practical help given by Professor Jørgen Fabricius, M.D. in solving technical and statistical problems have been of immense value and I wish to thank him for this.

Professor Bent Harvald, M.D., Torben Haghfelt, M.D. and Johannes Stræde Nielsen, M.D., Medical Department B, were always willing to give advice during the study.

I wish to thank Per Arnsbo and Petter Hermansen, engineers, who helped in the construction of the equipment as well as Jon Rasmussen, M.D., who willingly helped in the practical measurements. Further, Lise Hansen, M.Sc., who carried out the data processing.

The investigation would have been impossible without the ever-ready competent help provided by the nursing staff of the Medical Department B, especially that of Bodil Gammelgård. I would also like to express my gratitude to the staff of the Department of Clinical Physiology.

Secretaries Karen Eckhoff, Rita Ellegaard and Ellen Hansen have kindly given secretarial assistance in the preparation of the manuscripts.

Thanks are due to C.N. Harris, B.Sc., Ph.D. for propitious discussions during the translation.

The Danish Heart Foundation kindly provided financial support, particularly at the start of the investigation. Funds were also made available by the Danish Foundation for the Advancement of Medical Science and the Foundation for Medical Research in the County of Funen.

Finally I wish to express my gratitude to my family, Anne Katrin, Kristin and Marie Louise, for their encouragement during the whole period of the investigation.

October 1981.

Kristian Thygesen

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CHAPTER I

Introduction and object of the study.

The importance of infarct size.

The generally accepted view, that the high mortality during the early phase of acute myocardial infarction (AMI) is mainly due to ventricular arrhythmias, resulted in the establishment in the 1960's of Coronary Care Units (CCU). In these the use of monitoring technique combined with prompt antiarrhythmic treatment permitted previously fatal arrhythmias to be anticipated and treated (Oliver et al. 1967, Kimball and Killip 1968). The mortality of AMI patients during hospitalization in an ordinary medical ward was around 34-41% (Skall-Jensen 1967, Christiansen et al. 1971, Haghfelt 1971, Hofvendahl 1971), this fell to approximately 15-23% following treatment in a CCU (Nielsen 1970, Christiansen et al. 1971, Haghfelt 1971, Hofvendahl 1971, Helmers 1974, Thygesen et al. 1974). The residual mortality has remained more or less constant since and is caused in particular by pump failure (Kimball and Killip 1968, Swan et al. 1970).

It has been established with reasonable certainty that, in the absence of complicated lesions such

as ventricular septal defect or mitral regurgitation, the degree of pump failure is proportional to the extent of the damaged myocardium (Hood 1975). Heart failure will usually occur when 20-25% of the left ventricular wall is destroyed, while lesions involving more than 40% are accompanied by cardiogenic shock, usually with a fatal outcome (Harnarayan et al. 1970, Page et al. 1971, Hood 1975). Due to this, any treatment able to reduce the extent of the myocardial damage or prevent the evolution of the infarction will presumably be valuable, as it will reduce the risk of pump failure and with this the number of cases of congestive heart failure or cardiogenic shock (Maroko and Braunwald 1973). At the same time, it will presumably reduce the frequency of ventricular arrhythmias as the severity of these after myocardial infarction is related to the extent of the myocardial damage (Roberts et al. 1975b). Finally, such therapy by preserving the functional capacity of the myocardium may reduce the risk of the development of chronic heart failure, which is again related to a poor long term prognosis (Thygesen et al. 1977). However, before such interventions are adopted, it is quite essential, to be in possession of reliable methods for the evaluation of the evolution and extent of the infarction.

The concept of infarct size.

The term myocardial infarction is used to designate necrosis of heart muscle, secondary to a lack of blood supply (Chung and Duca 1975). The extent of an acute myocardial infarction is not predetermined by the nascent coronary ischaemia, but is the result of progressive dynamic processes, which pass through several characteristic stages (Jennings and Reimer 1973, Hood 1975, Kjekshus 1979). The duration of these stages depends on a balance between oxygen supply and oxygen consumption in the infarcted area (Maroko et al. 1971, Jennings and Reimer 1973). Cell damage occurring after an attack of myocardial ischaemia, is initially reversible, but later becomes irreversible unless more favourable metabolic or physiologic events improve the oxygen balance in the threatened area (Maroko and Braunwald 1973, Sobel 1975). However, it is not always possible to clearly distinguish, by means of measurements, between the stages reversibility = viability and irreversibility = non-viability (Hood 1975). It has been demonstrated experimentally, that irreversible cell damage after coronary occlusion can be detected within 20 to 120 minutes by electronmicroscopy, whereas 12 to 24 hours must pass before irreversibly injured cells become necrotic by both gross observation and light microscopic study, thereby enabling the histologic diagnosis of AMI to be made (Jennings and Reimer 1973). The extent of the myocardial infarction,

i.e. the volume of necrotic tissue cannot be precisely assessed until the necrotic changes have completely appeared (Sobel 1975). However, when viewed from the dynamic nature of the infarction process it would be preferable to employ the term infarct size for the extent of the irreversible ischaemic cell injury.

It is generally recognized that after experimental coronary occlusion the central area of ischaemic injury is surrounded by a partially ischaemic zone, the so-called twilight or border zone (Hearse et al. 1977, Banka et al. 1978, Harken et al. 1978, Helfant et al. 1978). This zone has been shown to be fairly narrow and characterized by maximum changes in flow, metabolism and electrophysiology (Hearse et al. 1978). However, it is conceivable that viable and salvageable myocardium may exist within the central zone as well as in the surrounding border zone; the extent of this salvageable area may depend on the time elapse after the coronary occlusion, myocardial oxygen requirements and the blood supply (Banka et al. 1978).

Despite the uncertain applicability of results from experimental myocardial infarction to clinical coronary artery disease, it is probable that concepts related to reversibility and to border zones are important clinically (Hood 1975). However, it should be borne in mind that clinical ischaemic lesions are

more complex and variable than their experimental counterparts, depending on factors such as: A) the location, severity and the rapidity of development of the coronary occlusion, B) the functional status of the other major coronary arteries as well as their anatomic pattern, particularly with regard to the areas of left ventricular myocardium supplied, C) the anatomic pattern and adequacy of the coronary collateral circulation (Hood 1975, Helfant et al. 1978). Consequently the exact measurement of infarct size would appear to be difficult due to the complexity of the natural history and individual components of the infarction process in man.

The assessment of infarct size.

Post mortem assessment of the magnitude of an infarction by macroscopic and light microscopic techniques have been known for many years (Mallory et al. 1939, Lodge-Patch 1951), but non-invasive methods are required in clinical investigations. Research in this area has been concentrated on electrocardiographic and other methods such as analysis of enzymes in the blood, radionuclide imaging of the myocardium and echocardiography.

Enzyme analysis.

An increased concentration in the blood of creatine kinase (CK), aspartate aminotransferase

(ASAT) and lactate dehydrogenase (LD) are used diagnostically in cases of AMI. The maximum values of the serum concentrations of these enzymes have been employed for clinical and prognostic studies of patients with AMI (Chapman 1971, Coodley 1973, Møller and Thygesen 1976, Thygesen et al. 1976). During the last decade models have been developed that allow a quantitative assessment of the infarct size from enzyme curves (Hørder et al. 1981). These have been based on experiments in animals (Kjekshus and Sobel 1970, Shell et al. 1971) and on assumptions regarding the turn-over in man of enzymes released from irreversibly injured myocardial tissue (Hørder et al. 1981). Various research centres have used these models, which in principle are based on the assumption of a one-compartment distribution space, in clinical trials regarding infarct size (Sobel and Shell 1972, Mathey et al. 1974, Norris et al. 1975, Roberts et al. 1975a). However, criticism has been raised against these one-compartment models, which are very sensitive to variations in the parameters employed in the formulae, and which are in addition an over-simplification of a very complex biological system (Roe and Starmer 1975, Roe 1977, Hørder et al. 1981). Therefore, it has recently been suggested that other models e.g. two-compartment models should be employed, which from a physiological point of view should provide a more valid evaluation of the extent of enzyme release from infarcted heart tissue (Witteveen et al. 1975, Sobel et al. 1977, Petersen et al. 1981).

Radionuclide imaging.

Radio-isotopes have been used in the diagnosis of AMI as well as for the evaluation of the infarct size. The isotopes employed can be divided into two classes: 1) isotopes which accumulate in ischaemic or infarcted myocardium, from which a positive infarct scintigram can be obtained ("hot scan"): examples of these are technetium - ^{99m}Tc complexes, where ^{99m}Tc -pyrophosphate is that most commonly employed (Lessem 1979). However, these techniques do not appear to be sensitive until 12 to 24 hours after the onset of the infarction, which in itself prevents the early prediction of the infarct size, and a half-life of 6 hours for ^{99m}Tc is a further limiting factor if serial scanning is contemplated in order to follow infarct evolution (Holman 1976). 2) Isotopes reflecting the regional perfusion accumulate in normal myocardium thus producing a negative infarct scintigram ("cold scan"); examples are potassium-43, and its analogues cesium-129, rubidium-81 and thallium-201 (Lessem 1979). Scar tissue after previous infarction or other types of hypoperfused tissue do not take-up these radionuclides, and for this reason a negative scintigram is not infarct-specific. An infarcted area can be discovered very early by means of these agents, but their long half-life and the high patient dosage prejudice the use of serial scanning in the early phase

of AMI (Holman 1976). Newer and more advanced imaging techniques are being developed at present, including emission and transmission computerized axial tomography (Adams et al. 1976, Weiss et al. 1977).

Echocardiography.

Echocardiography is a technique, which is capable of detecting abnormal segmental wall motion during myocardial ischaemia (Waters and Forrester 1978). However, M-mode and two-dimensional echocardiography are of limited value when used to assess the extent of ischaemia, since not all regions of the left ventricle can be adequately visualized (Waters and Forrester 1978, Eaton et al. 1979). A three-dimensional technique has been developed, which is said to be useful for the estimation of infarct size (Nieminen and Heikkilä 1979).

The electrocardiographic assessment of infarct size.

The electrocardiogram (ECG) is subject to a number of characteristic changes during the evolution of a myocardial infarction. The elevation of the ST segment is presumed to reflect severe ischaemic injury to the myocardial cell (Rakita et al. 1954, Prinzmetal et al. 1961, Goldberger 1975). It is further generally accepted that the appearance of an abnormal Q wave and a reduction in height of the R wave are caused by a loss

of membrane potential as a result of the occurrence of non-viable myocardial tissue (Johnston et al. 1935, Wilson et al. 1935, Maxwell et al. 1954, Shaw et al. 1954, Banka et al. 1978). Definite changes of these electrocardiographic components in the 12 standard leads play an important role in the establishment of the diagnosis AMI according to the criteria of WHO (Working group 1971), and can, in addition, be used for a clinical and prognostic evaluation of patients with AMI (Nielsen 1973, Wilson and Pantridge 1973, Morris et al. 1974, Thygesen et al. 1974, Gottlieb et al. 1975, Mills et al. 1975, Askenazi et al. 1978). The basis for a more quantitative employment of the ECG for the estimation of infarct size was made in experimental studies with multiple epicardial ECG-leads (epicardial ECG-mapping), where it was demonstrated that the number and the sum of leads with early ST elevation was related to the extent and severity of the acute ischaemic injury (Maroko et al. 1971, Kjekshus et al. 1972). Later it was shown that changes in the epicardial QRS complex correlate closely with the amount of necrosis in the subjacent myocardium (Muller et al. 1975, Hillis et al. 1976). Further, it was demonstrated by means of simultaneous ECG recordings, using multiple epicardial and praecordial leads, that changes in epicardial potentials are closely reflected by changes in praecordial potentials (Wilson et

al. 1944, Muller et al. 1975). With this the electrophysiological rationale was present for the use of multiple praecordial ECG-leads (praecordial ECG-mapping) for the assessment of infarct size. In the pioneer stage of praecordial ECG-mapping, only the ST segment was analyzed (Reid et al. 1971, Maroko et al. 1972, Reid et al. 1974, Madias et al. 1975), but later changes in the QRS complexes were also included (Essen et al. 1977, Selwyn et al. 1977b, Awan et al. 1977, Henning et al. 1978, Muller et al. 1978, Rubenstein and Freitas 1978, Yusuf et al. 1978).

However, there is some controversy as to the significance and usefulness of the ECG-mapping technique, especially that of ST segment mapping for the assessment of myocardial injury (Corday 1976, Meerbaum and Corday 1977). It has been suggested from the theoretical and experimental bases of ST segment deviation that ST segment mapping is not a reliable measure of myocardial ischaemia (Holland and Brooks 1975, Fozzard and DasGupta 1976). Other investigators have pointed out the limitations of this method when used for the bedside estimation of ischaemic injury (Norris et al. 1975, Thompson and Katavatis 1976). Corresponding criticism will probably be raised to the use of Q and R waves for infarct sizing when these become more generally employed.

It is essential to acquire thorough knowledge of the methodologic and spontaneous variations

in the ST segment, Q and R waves in order to ascertain whether these may be employed quantitatively, qualitatively or not at all for the assessment of infarct size.

Object of the study.

The object of the present investigation has been to study and evaluate in patients with and without AMI:

- 1) the reliability of the measurements of the ST segment elevation and the amplitude of Q and R waves in the surface ECG. Due regard being taken to noise from the experimental set-up (error-of-measurement) and "biological" noise (background noise).
- 2) the variability of the ST elevation and the Q and R amplitudes, including the relationship of these signals during infarction to background noise (signal to noise ratio).
- 3) the evolution of the ST elevation and the Q and R waves after an infarction; further, the possibility of predicting the development of Q and R waves from the early ST elevation.
- 4) the correlation between ST elevation and clinical parameters e.g. heart rate, blood pressure, respiratory rate, oxygen treatment and chest pain.
- 5) the application and limitation of surface ECG recordings when using one or multiple leads, as well as the

usefulness of praecordial ECG-mapping for the estimation of infarct size.

The project fell into two parts. In the first the electrocardiographic signals were measured in a single lead (articles I and II, chapter III), in the second in 42 praecordial leads (articles III and IV, chapter IV).

CHAPTER II

Theoretical basis of changes in the ST segment and the QRS complex.

ST segment changes after coronary occlusion.

It has been known for approximately 60 years that ST elevation can be an electrocardiographic sign of coronary artery occlusion (Pardee 1920). After experimental occlusion, the ST segment becomes elevated within 1 minute to a maximum within 10 to 20 minutes, followed by a gradual fall (Rakita et al. 1954, Maroko et al. 1971, Yamada et al. 1972, Hirsfeld et al. 1974, Khuri et al. 1975, Vincent et al. 1977, Selwyn et al. 1978c).

The electrophysiological basis of ST segment deviation.

Several theories have been put forward regarding the changes in the ST segment during myocardial ischaemia. These are based on the assumption that ischaemic and normal cells have different membrane potentials, permitting currents of injury to flow across the boundary between damaged and normal cells (Samson and Scher 1960, Caskey and Estes 1964, Goldberger 1975, Ross 1976, Hillis and Braunwald 1977, Holland and Brooks 1977, Vincent et al. 1977).

Currents of injury.

According to one theory during the electric diastole the damaged cells have a lower membrane potential than normal cells, this results in a diastolic current flowing from the damaged to the normal tissue (Samson and Scher 1960, Prinzmetal et al. 1961, Vincent et al. 1977, Kléber et al. 1978). According to other theories, during the repolarization portion of systole, the membrane potentials of the ischaemic cells become negative earlier than those of the normal cells, either because of incomplete depolarization and/or accelerated early repolarization; this results in a systolic current flowing from normal to damaged tissue (Samson and Scher 1960, Holland and Brooks 1977, Vincent et al. 1977, Kléber et al. 1978). The diastolic current of injury causes a depression of the TQ segment in the leads overlying the area of ischaemia, while the systolic current of injury is reversed and causes the ST segment in the same leads to become elevated; both of these changes are registered as ST elevation when using conventional electrocardiographs equipped with a baseline compensator, which does not differentiate between TQ segment depression and true ST segment elevation (Samson and Scher 1960, Bruyneel 1975, Goldberger 1975, Holland and Brooks 1977, Vincent et al. 1977). The relative contribution of each of these diastolic and systolic components to the total ST segment

displacement has not yet been fully elucidated (Samson and Scher 1960, Caskey and Estes 1964, Goldberger 1975, Ross 1976, Hillis and Braunwald 1977, Holland and Brooks 1977), but recent studies suggest that the contribution is time-dependent and that the TQ segment depression is likely to play the dominant role, whereas the true ST segment elevation is a more unspecific indicator of ischaemia (Yamada et al. 1972, Cohen and Kaufman 1975, Vincent et al. 1977, Kléber et al. 1978). The non-specificity of true ST elevation may be of importance in infarct sizing when using conventional electrocardiographs. Further, it is possible that an intervention may alter the true ST elevation without actually modifying the severity or extent of ischaemic injury (Vincent et al. 1977).

Ion transport across the cell membranes.

An altered ion transport across the cell membranes appears to be the most probable basic cause of changes in the injury current responsible for the ST segment displacement during myocardial ischaemia (Prinzmetal et al. 1961, Surawicz 1967, Goldberger 1975, Ross 1976, Hillis and Braunwald 1977, Holland and Brooks 1977, Kjekshus 1979). A metabolic dependent active sodium pump, situated on the cell membrane, ensures a high intracellular concentration of potassium and a high extracellular concentration of sodium (Leaf 1970,

Goldberger 1975). It has been postulated that during ischaemia the amount of energy available for this pump is reduced, resulting in a sodium accumulation intracellularly and potassium leakage to the extracellular space. The consequence of these ionic shifts is a hypopolarization of the cell membrane, depicted as an elevation of the ST segment, which is caused by a compensated negative shift of the TQ segment (Prinzmetal et al. 1961, Goldberger 1975, Bodenheimer et al. 1976a, Holland and Brooks 1977). It has also been observed experimentally, that perfusion of the myocardium with solutions having a high potassium concentration leads to hypopolarization of the cell membranes, with a resulting ST elevation. In contrast, a wash-out of extracellular potassium in the ischaemic area will produce a reduction in the ST elevation (Prinzmetal et al. 1961, Goldberger 1975, Kjekshus 1979). Non-ischaemic changes in TQ-ST shift can thus occur following changes in the ionic concentration, particularly in the concentration of potassium, as well as with interventions which interfere with the ionic pump, such as digitalis, quinidine and sympathetic stimulation (Ross 1976, Kjekshus 1979).

The ST segment displacement resulting from ischaemic cell injury and non-ischaemic factors can also be expressed in vectorial terms (Beckwith 1970). A more detailed description of the vectorial theory is given under the heading: The electrophysiological basis of QRS changes.

Ischaemic and other causes of ST segment deviation.

An increasing elevation of the epicardial ST segment has been observed in numerous investigations when the area of ischaemia is enlarged (Maroko et al. 1971, Maroko et al. 1972a-e, Redwood et al. 1972, Kjekshus and Mjøs 1973, Muller et al. 1975, Smith et al. 1975, Mjøs et al. 1976). However, it has also been reported that ST elevation can decrease in the central zone of an area with ischaemic injury, when this becomes more ischaemic and enlarged by additional coronary ligations (Cohen and Kirk 1974, Muller et al. 1975). There is some controversy as to the cause of this paradoxical reduction in the epicardial ST elevation. It is thus maintained that the reduction is due to the development of local intramyocardial conduction delay in the centre of large areas of severe ischaemia (Muller et al. 1975), inasmuch as secondary changes in the ST segment due to prolongation of the QRS complex can be explained by the ventricular gradient and vectorial theories (Ashman and Byer 1943, Beckwith 1970). But in another investigation it was found that intramyocardial conduction delay was seldom pronounced in the early stages of myocardial ischaemia (Heng et al. 1976). On the other hand reduction in the epicardial ST elevation has been explained geometrically by Holland and Brooks (1975), who postulate by means of solid angle analysis that a reduction in the epicardial ST elevation does not necessarily indicate a reduction in the extent of the ischaemic injury. Thus

the ST segment changes are affected by the placement and orientation of the recording electrodes in relation to the geometry of the ischaemic region, as well as by the size, severity and duration of the ischaemic process (Holland and Brooks 1975).

However, it must be emphasized that these findings do not invalidate the fact that ST elevation does occur with acute myocardial ischaemia, both in animal experiments and in patients, and that it can therefore be employed for the detection of new episodes of ischaemic injury, providing non-ischaemic causes of ST segment deviations are excluded (Heng et al. 1976, Ross 1976, Muller et al. 1978, Kjekshus 1979). These non-ischaemic factors, of which a number have already been mentioned, include changes in temperature, pH and ionic concentration, drugs such as quinidine, digitalis and beta adrenergic blocking agents, the presence of ventricular conduction defects and ventricular hypertrophy, sympathetic stimulation of the heart, epicardial injury due to pericarditis, and early repolarization variants (Goldberger 1975, Braunwald and Maroko 1976, Ross 1976).

ST segment changes related to coronary blood flow.

No simple quantitative relationship exists between ST segment elevation and a reduction in the regional myocardial blood flow after coronary occlusion (Becker et al. 1973, Timogiannakis et al. 1974,

Smith et al. 1975, Ross 1976, Irvin and Cobb 1977). It has been demonstrated experimentally, that a fall in the coronary blood flow from one half to two thirds always produces changes of the ST segment, whereas a lesser decrease only causes slight or no changes (Wegria et al. 1949, Lekven et al. 1975, Irvin and Cobb 1977). The observation was made that within 15 minutes to 2 hours after occlusion there was only a weak negative correlation between myocardial flow and epicardial ST elevation, or in other words there was considerable variation in the levels of the ST elevation for a given blood flow (Smith et al. 1975, Heng et al. 1976, Irvin and Cobb 1977). A further study showed a linear relationship between the epicardial ST elevation 15 minutes after occlusion and a reduction in the subepicardial blood flow 24 hours later, but the relation between ST elevation at 15 minutes and the subendocardial blood flow was nonlinear (Kjekshus et al. 1972). This variable relationship between regional myocardial blood flow and ST elevation may be due to differing collateral blood flows (Pasyk et al. 1971, Hirzel et al. 1976), but irrespective of the cause of the discrepancy between ST elevation and regional blood flow, it is obvious that ST segment analysis cannot be designed to monitor myocardial blood flow (Surawics 1977).

ST segment changes related to myocardial metabolism.

There is some evidence that the height of the epicardial ST elevation is correlated to changes in the myocardial metabolism caused by the ischaemia (Maroko et al. 1971, Hillis and Braunwald 1977, Muller et al. 1978). An accumulation of lactate has been found in areas with ST elevation (Scheuer and Brachfeld 1966, Karlsson et al. 1973) together with significantly lower concentrations of adenosine triphosphate (ATP) and creatine phosphate (CP) (Karlsson et al. 1973). However, there is no precise quantitative relation between the grade of ST elevation and the amount of lactate accumulation or ATP and CP deficit; further, a slight lactate accumulation and ATP and CP depletion were sometimes observed in areas with no ST elevation adjacent to the ischaemic region (Karlsson et al. 1973). Finally, it has been demonstrated that the intramyocardial oxygen tension is related to the ST elevation recorded both epi- and intramyocardial (Sayen et al. 1961, Angell et al. 1975, Khuri et al. 1975).

ST segment changes related to enzyme and structural changes.

A relation has been observed in several experimental studies between epicardial ST elevation 15 minutes after coronary artery occlusion and myocardial CK depletion at 24 hours (Maroko et al. 1971, Kjekshus

et al. 1972, Radvany et al. 1975, Heng et al. 1976).

This correlation was good in some of the studies (Maroko et al. 1971, Kjekshus et al. 1972) but poor in others (Heng et al. 1976). Thus, there is no precise quantitative relationship between the early ST elevation and the severity of the ultimate myocardial damage as judged by tissue CK depletion (Heng et al. 1976). Neither was it possible to demonstrate a consistent quantitative relationship between ST elevation and ultrastructural myocardial injury in a study where the epicardial ST segment changes 20 minutes after coronary artery occlusion were related to the transmural morphological changes, as detected by electron microscopy of tissue samples taken at the same time. Thus, prominent ST elevation in ischaemic zones always indicates the presence of underlying structural changes, but marked changes could also be present when ST elevation was minimal, indicating that ST segment changes tend to underestimate the extent of early ischaemic damage (Lamberti et al. 1978).

The significance of electrode position for ST elevation.

The intramyocardial ST segment is a more sensitive indicator of myocardial ischaemia than the epicardial ST segment, which in turn is superior to that recorded from the praecordium. Furthermore, the ST segment, either epicardial or praecordial, is a more

sensitive reflection of subepicardial than of subendocardial ischaemia (Braunwald and Maroko 1976, Ross 1976, Hillis and Braunwald 1977, Muller et al. 1978). The interpretation of the ST elevation in epicardial and praecordial leads may be additionally complicated by the effects of reciprocal changes in the ST segment vector (Muller et al. 1975, Braunwald and Maroko 1976, Ross 1976). Praecordial ST segment mapping can therefore at the very best only be expected to demonstrate changes in the surface area and not the mass of the infarcted myocardium (Surawics 1977).

Despite these limitations an analysis of the ST elevation provides a useful indicator of alterations in ischaemic injury in the early phase after coronary occlusion (Braunwald and Maroko 1976, Ross 1976, Muller et al. 1978, Kjekshus 1979). A reduction in the magnitude of the ST elevation may result from one of two things either improvement in the condition (reversible ischaemia) or deterioration (irreversible damage). Consequently, ST segment mapping cannot be used alone as an electrocardiographic method for the evaluation of infarct evolution. Therefore, it has been suggested that an analysis of concomittant changes in the QRS complex may enhance the usefulness of the method (Braunwald and Maroko 1976, Ross 1976, Hillis and Braunwald 1977, Muller et al. 1978, Kjekshus 1979).

QRS changes after coronary occlusion.

Some 50 years ago it was observed that the development of a Q wave was a diagnostic sign of AMI (Levine and Brown 1929, Pardee 1930, Fenichel and Kugell 1931). After experimental coronary occlusion it has been shown that Q waves appear progressively from the endocardium to epicardium (Banka et al. 1978). After one hour, local electrographic Q waves are seen in the endocardial layers only (Banka et al. 1978). After 3-4 hours the Q waves have spread transmurally, being visualized in both endocardium and epicardium (Banka et al. 1978, Mickleborough et al. 1978). Immediately after coronary ligation, giant R waves may develop in severely ischaemic areas (Ekmekci et al. 1961, Prinzmetal et al. 1961, Selwyn et al. 1978d), but these are probably the result of delayed conduction in the area of ischaemia (Ekmekci et al. 1961, Prinzmetal et al. 1961). Apart from this initial R wave increase, it has been shown that the epicardial R waves are significantly reduced within one hour (Johnston et al. 1935, Muller et al. 1975, Banka et al. 1978, Selwyn et al. 1978d). This reduction also occurs in the endocardial electrogram, even though the R waves here are much smaller than those in the epicardial electrogram (Banka et al. 1978). The reduction in the epicardial R waves continues, though to a lesser degree between one and 4 hours (Johnston et al. 1935, Banka et

al. 1978, Selwyn et al. 1978d). After 5 hours the decrease in the R waves and the development of the Q waves over the infarcted area are complete (Selwyn et al. 1978d).

The electrophysiological basis of QRS changes.

Two general theoretical approaches have been postulated to explain the changes in the QRS complex during infarction, the one is the classic cavity potential theory with later modifications and the other, the vectorial theory.

Cavity potential theory.

When the myocardium beneath an electrode is dead, it does not respond to the excitatory process and the negative potential of the ventricular cavity (QS) is transmitted through the electrically inert myocardium to the overlying electrode. If electrically viable tissue remains in the infarcted area, it may produce notched QS complexes or the pattern may become different types of QR complexes (Johnston et al. 1935, Wilson et al. 1935a,b, Wilson et al. 1944, Wilson et al. 1947).

The theory of transmural Q waves has later been supported by others (Shaw et al. 1954, Prinzmetal et al. 1954b, Maxwell et al. 1954, Durrer et al. 1964). However, QS waves have also been seen in non-transmural infarctions, namely, when the subepicardium was damaged and the subendocardium intact (Shaw et al. 1954, Maxwell et al.

1954). The explanation of this is presumed to be that depolarization occurs so rapidly in the endocardium that it does not appear in the ECG (electrical silent subendocardium) (Prinzmetal et al. 1954a, Shaw et al. 1954, Massumi et al. 1955, Sodi-Pallares et al. 1961). Activation of the outer ventricular layer is primarily responsible for the R wave, when recording over the normal heart, and it follows that an R wave will not occur if the subepicardium is inactivated. Conversely, unless the subepicardium is at least partially inactivated, an abnormal Q wave will not occur. Hence a mixture of electrically active and inactive tissue in the subepicardium is necessary to yield QR waves, and thus pure subendocardial infarctions will not produce changes in the QRS complex of the ECG (silent subendocardium) (Shaw et al. 1954).

The concept of an absence of Q waves in cases of subendocardial infarctions has not been validated in other investigations. Thus, definite Q waves have been found in the ECG in post mortem studies of patients with infarctions limited to the subendocardium (Wilkinson et al. 1963, Savage et al. 1976, Raunio et al. 1979), and experimentally it has been found that subendocardial infarctions and scars can produce Q waves in the epicardial electrogram and surface ECG (Durrer et al. 1964, Boineau et al. 1968). These conflicting views on the presence of Q waves with subendocardial infarction may perhaps

be explained by different electrode positioning and the site and size of the infarction (Wilson et al. 1947, Boineau et al. 1968, Holland and Arnsdorf 1977). In this context the distribution of Purkinje fibres may play a role (Goldman 1976). Thus it is postulated that the electrically silent endocardial areas are those in which Purkinje fibres penetrate deeply into the myocardium. In those areas where the fibres are absent or very scarce, the endocardium will generate a R wave under normal conditions, and in such an area endocardial infarction can produce an abnormal Q wave in a surface lead (Sodi-Pallares et al. 1961, Goldman 1976).

Vectorial theory.

Changes in the QRS complex (as well as in the ST segment) can be conceptualized in vectorial terms as a balance between positive and negative electromotive forces (Goldberger 1975, Goldman 1976). The deflections of the ECG represent a spatial and temporal summation of electrical activity of all regions of the heart (Beckwith 1970). A Q wave in any given lead indicates that the net vectorial sum of the initial depolarization forces is negative. Infarctional Q waves are considered, irrespective of the lead, to be the result of a loss of myocardial forces as a consequence of ischaemic injury (Beckwith 1970, Goldberger 1975). The vectorial theory states that a loss of electromotive forces in one direction will

produce a reciprocal gain in the potentials of the opposite direction. For example, when a strictly posterior infarction occurs, huge R waves appear in the praecordial leads, which cannot be explained by the cavity theory (Goldberger 1975).

The vectorial model has the additional advantage that it can explain the occurrence of non-infarctional Q waves. Thus, these may not only occur with a net decrease of positive forces as seen with myocardial injury, but also from a net increase of negative forces as seen for example in cases of cardiac hypertrophy (Goldberger 1975).

Non-infarctional causes of QRS changes.

As mentioned above, the QRS complex can be modified not only by myocardial infarction but also by other factors. Changes in the QRS may be due to cardiac orientation. Q waves as normal variants may appear in certain leads (e.g. III, aVL, aVF, V_1 and V_2) depending on the position of the heart. Such positional pseudo-infarctional patterns are also found in dextrocardia and very occasionally in cases of pectus excavatum (Goldberger 1975, Holland and Arnsdorf 1977). Pseudoinfarctional patterns can also occur with hypertrophy and dilatation of the heart and due to altered ventricular conduction (Wilson et al. 1947, Goldberger 1975, Holland and Arnsdorf

1977). In addition pseudoinfarctional Q waves can be present in cases of myocardial injury such as myocarditis and conditions in which the myocardium is replaced by electrically inert tissue, for example tumour, sarcoidosis and fibrous tissue (Goldberger 1975).

Q waves can appear transiently and do not necessarily signify irreversible damage to the heart muscle (Goldman et al. 1960, DePasquale et al. 1964, Helfant 1976). It has been shown experimentally that short periods of coronary occlusion produce transient Q waves in dogs without subsequent evidence of myocardial damage at autopsy (Bayley and LaDue 1944, Gross et al. 1964). Clinically, transient Q waves have also been documented in the context of pronounced hyperkalaemia, coronary insufficiency, angina pectoris, shock, tachyarrhythmias and with open heart surgery as well as in cases of old infarction (Wilson et al. 1944, Roesler and Dressler 1954, Rubin et al. 1963, DePasquale et al. 1964, Mamlin et al. 1964, Shugoll 1967, Klein et al. 1970, Bassan et al. 1974, Helfant 1976).

An evaluation of the changes in the QRS complex in cases of AMI is more difficult or even impossible in the presence of pseudoinfarctional or old infarction patterns. These conditions should thus be eliminated if possible from studies where the development of the Q wave or loss of R wave are used for monitoring the evolution of the infarction. Further, in cases with

reversibility of the Q wave, this cannot be employed as an indicator of necrosis. But apart from cases of conduction abnormalities Q wave reversal in patients with AMI is extremely rare, and when it does occur, is present only for a short time; Q wave reversal is therefore unlikely to influence ECG-mapping results (Muller et al. 1978).

QRS changes related to enzyme and structural changes.

A close correlation has been seen experimentally between QRS changes in the epicardial electrogram and the extent of necrosis of the subjacent myocardium, as measured biochemically and histologically (Hillis and Braunwald 1977). Thus, there is not only a relationship between the presence of epicardial Q waves and the levels of myocardial CK at 24 hours after coronary occlusion (Heng et al. 1976), but also a correlation between Q wave development (ΔQ), R wave fall (ΔR) and their combination $\Delta(Q+R)$ at 24 hours and the myocardial CK depletion and the histologic severity of necrosis, respectively (Hillis et al. 1976). It has also been found that epicardial $\Delta(Q+R)$ at 5 hours was closely correlated to myocardial depletion of CK activity at 24 hours (Selwyn et al. 1978d). Therefore, QRS changes provide not only evidence concerning the irreversible loss of active myocardium (Selwyn et al. 1978d), but they are also an important time indicator giving direct information regarding the progress of a myocardial infarction.

The significance of electrode position for infarctional Q waves.

It has been demonstrated, both in animal studies and in patients, that the praecordial ECG is less sensitive for the detection of infarction than the epicardial electrogram as an infarction must be of a certain volume to produce a Q wave on the epicardium and larger still to create a Q wave in the distant chest ECG (Cook et al. 1958a-b, Durrer et al. 1961, Daniel et al. 1971, Bodenheimer et al. 1976b, Holland and Arnsdorff 1977). Consequently a simple quantitative relation between infarct size and QRS alterations cannot be expected in the praecordial ECG.

ST segment elevation related to QRS changes.

A relationship has been demonstrated experimentally between epicardial ST elevation at 15 to 17 minutes after occlusion and the development of Q waves as well as the reduction of R waves at 2 - 6 and at 24 hours (Hillis et al. 1976, Selwyn et al. 1978d). It has been suggested that this observation could be used clinically for the prediction of the development of Q waves and the fall in the R waves from the early ST elevation in praecordial leads (Askenazi et al. 1977, Maroko et al. 1977, Selwyn et al. 1978c).

Such an analysis should theoretically be able to: 1) predict the surface area of the expected

irreversible injury during the reversible phase, i.e. while ST elevation is present but before changes in the QRS complex have developed and 2) estimate the surface area of this irreversible injury that has actually developed, as reflected by changes in the QRS complex (Askenazi et al. 1977, Maroko et al. 1977).

CHAPTER III

The use of a single surface unipolar lead.

Study groups.

Thirty patients, who were admitted to the Coronary Care Unit (CCU) on average 2 hours (range $\frac{1}{2}$ - 10) after the onset of symptoms (i.e. retrosternal pain of more than 20 min duration), were studied (I). The patients were selected inasmuch as a ST elevation of ≥ 2 mm in one or more leads $V_1 - V_6$ was required in cases of anterior AMI (14 patients) and ≥ 1 mm in leads III and aVF with inferior AMI (16 patients). Their average age was 63 years (range 44 - 80), 22 were men and 8 women. Patients with pericarditis, disturbances of electrolyte balance, a QRS duration ≥ 0.12 sec, ECG signs of ventricular hypertrophy or strain, or patients on drug therapy possibly affecting the ST segment or QRS complex (digitalis, quinidine, isoproterenol, verapamil, β -adrenergic blocking drugs) were not admitted to the study. The diagnosis AMI was established according to the criteria of WHO, as all the patients developed definite signs of infarction (pathological Q waves) in the routine ECG recording, and all had, in addition, a

diagnostic rise in serum enzymes CK, ASAT and LD (Working group 1971). Twenty-seven of the patients had their first AMI, while 3 had their second infarction⁷ (no old infarct pattern in the affected area).

The patients were treated according to the usual procedure of the CCU (I). Two patients were treated during the period of observation with digoxin from the 12th and 46th hours after admission and measurements after these points are not included in the analyses. One patient developed pericarditis 49 hours after admission, but this occurred after the cessation of measurements. Based on the clinical classification of heart failure in patient with AMI (Killip and Kimball 1967), 2 patients had no signs of cardiac failure, 25 had mild to moderate heart failure (lung stasis), 3 had pulmonary oedema, while none suffered from cardiogenic shock (I). Three patients died during the period under study, two 10 hours and one 41 hours after admission.

The control group comprised 25 patients, of these 20 were admitted with chest pain but with no indication of AMI, and 5 because of extra-cardiac disease (I). Their average age was 49 years (range 18-77), and there were 18 men and 7 women. All the patients gave their informed consent.

Comments

In order to evaluate the spontaneous development and variations in ECG components after AMI, the patients were selected, employing certain criteria. The presence of factors or conditions, known to affect the ECG components (apart from AMI) were not included in the study groups. As the investigation was designed to study the ECG changes occurring from the very beginning after the infarction the patients with a very short duration of symptoms and a characteristic ST elevation were selected.

Despite these selection criteria, the results obtained from the present patient sample should be considered applicable for AMI patients in general. The age and sex distributions of the sample are similar to these of large patient materials reported earlier from this CCU (Nielsen 1970, 1973, Thygesen et al. 1974, Nielsen 1975, Thygesen et al. 1977). The frequency of heart failure in the above mentioned patient series was 72 - 78% (Nielsen 1973, Nielsen 1975, Thygesen et al. 1977) while that of cardiogenic shock was 11 - 14% (Nielsen 1970, 1973), which roughly correspond to figures given elsewhere (Brest 1975, Yu 1975); furthermore, the acute mortality was 15 - 23% (Nielsen 1970, Thygesen et al. 1974). It is possible that the frequency of congestive heart failure in the sample is a little too high, but on the other hand, there were no cases of cardiogenic shock and in addition, the mortality was somewhat lower.

The control groups consisted, in the main, of patients with chest pain but no indications of AMI, and were thus suitable for comparing the ECG signals in patients with and without AMI. Both groups were, on the whole, comparable with regard to age and sex distribution.

The method.

In 14 patients with anterior AMI the site showing the highest initial ST elevation was selected from 42 praecordial sites (I). An electrode (Red Dot adhesive silver/silver chloride electrode) was attached to this site and an ECG recorded every hour for the following 48 hours after the onset of the infarction. In 16 patients with inferior AMI an ECG was recorded every hour for 48 hours using lead aVF. In the control group, where the ECG was recorded every hour for 24 hours, the praecordial lead corresponding to V_3 was employed in 15 patients, while lead aVF was used in the remaining 10 patients (I).

The electrocardiograph was a Siemens-Elema Mingograph 34 with a paper speed of 50 mm/sec and calibrated to 1 mV = 10 mm. The ECG complexes were analyzed by means of a Hewlett Packard 9864A digitizer/9810A calculator. The duration of the Q and QRS complexes as well as the amplitude of Q (QS) and R waves and the

deviation of the ST segment 60 msec after the nadir of the last wave, usually the S wave, were calculated as the arithmetic mean of 3 consecutive ECG complexes. The heart rate was calculated as the harmonic mean using three adjacent intervals. The PQ level was employed as the base line. Q (QS) and R waves were identified by means of the Minnesota code criteria (Rose and Blackburn 1968). The measured values of the amplitudes of Q (QS) and R waves as well as the ST segment deviation were only included in the final calculation if the QRS duration was < 120 msec (I and II).

Comments

The measuring set-up should comply with two requirements: 1) the out-going signal from the measuring instrument must reflect unambiguously and with the desired exactitude the course of the process being studied. 2) The measuring equipment should affect the object to be measured to the least possible extent. The likelihood of interaction between the object and the measuring equipment should always be borne in mind (Sten-Knudsen and Nissen-Petersen 1973).

As the ECG was recorded from the body surface it must be presumed that the recording equipment will have no or little effect on the potentials of the myocardial cells. On the other hand, due to the considerable

distance between heart and electrode and even further to the actual print-out, it is necessary to have a thorough knowledge of the signal to noise ratio when evaluating an ECG. Therefore, the electrocardiographic infarction signals, which are registered in a surface ECG must be evaluated partly in relation to the noise from the experimental set-up (error-of-measurement), and partly in relation to the "biological noise" (background noise) which is present in every individual (Simonson et al. 1949).

The reliability of the measurements.

The random error following registration of the ST segment as well as the Q and R waves in the surface ECG's will be termed in the following: error-of-measurement. Various important variance components which are included in the error-of-measurement, following the use of a single praecordial unipolar lead, are shown in Table I. These are intra-observer, inter-observer and electrocardiographic replacement variations, which were expressed by the pooled standard deviation (PSD), calculated from double determinations of the stated electrocardiographic components. The procedure employed for determining the PSD of both the Q and R waves was similar to that used for the ST segment deviation (I). The highest calculated PSD's were employed as an estimate of the error-of-measurement of the method using a single

Table I. Estimates of variance components (intra-observer, inter-observer, electrocardiograph replacement) according to errors in a single praecordial unipolar lead. The estimates are expressed as PSD, each based on 20 replicates.

	Pooled standard deviation (mm)		
	Intra-observer	Inter-observer	Electrocardiograph replacement
ST segment deviation	0.18	0.16	0.15
Q wave amplitude	0.16	0.17	0.70*
R wave amplitude	0.18	0.13	0.63

* based on 8 replicates.

praecordial lead: for ST deviation the PSD = 0.18 mm (coefficient of variation (CV) = 4.4%), Q wave the PSD = 0.70 mm (CV = 5.3%) and R wave the PSD = 0.63 mm (CV = 7.3%). Other components of the measuring set-up, which could possibly influence the error-of-measurement, have recently been demonstrated as playing a negligible role; thus measurement of a set length with a digitizer was extremely precise, also after replacement of the ECG-paper (I).

The calculated PSD's for the hour-to-hour variation were used as the estimate for the intra-individual variation of the control patients, these include the error-of-measurement. In Table II can be seen the PSD's for the ST segment, Q and R waves, respectively, in lead V_3 and lead aVF; no Q waves were registered in lead V_3 of the control group. The upper limit of normal for the hour-to-hour variations in deviation and amplitude were based on the

Table II. Estimates of intra-individual variation (hour-to-hour variation) of the electrocardiographic components in control patients in lead V_3 ($n = 15$) and lead aVF ($n = 10$), respectively.

	Pooled standard deviation (mm)	
	Hour-to-hour variation	
	Lead V_3	Lead aVF
ST segment deviation	0.26	0.18
Q wave amplitude	-	0.30*
R wave amplitude	1.08	0.88

* based on $n = 6$.

95 per cent confidence interval and have been termed the maximum permissible hour-to-hour or intra-individual variation. This was calculated by means of the one-tailed test of the normal distribution as the determination of the upper limit was of sole interest (Michaels and Cadoret 1967). Thus, the maximum permissible intra-individual variation on measurement of the ST segment deviation was 0.4 mm and 0.3 mm in V_3 and aVF, respectively, on measurement of the Q amplitude of 0.5 mm in aVF, and on measurement of the R wave amplitude of 1.8 mm and 1.4 mm in V_3 and aVF, respectively.

Anatomical and physiological changes in the position of thoracic structures influence the orientation of the heart and are thus indirectly reflected in the configuration of the ECG (Goldberger 1975, Selwyn and Shillingford 1977). A systematic study of this phenomenon was carried out by changing the

position of the patient (I). The errors brought about in this manner were termed induced measuring errors, and these include the error-of-measurement.

Table III. Estimates of variance components (various patient positions) of induced measuring errors in a single surface unipolar lead. The estimates are expressed as PSD, each value based on 20 paired measurements in the indicated position and the supine position.

	Pooled standard deviation (mm)			
	Lead V_3		Lead aVF	
	Left oblique	Right oblique	Left oblique	Right oblique
ST segment deviation	0.24	0.21	0.15	0.15
Q wave amplitude	5.66*	1.38*	0.20	0.29
R wave amplitude	0.75	1.30	0.50	0.98

* based on 8 replicates.

Table III shows the components of variance in a single surface unipolar lead in various patient positions, expressed by the PSD, calculated from 20 paired comparisons: the indicated position versus the supine position. With the exception of the Q wave in lead V_3 , it was found that the induced measuring errors of the electrocardiographic components were of the same magnitude as the intra-individual variation of these in the control groups. There was a pronounced induced measuring error with regard to the Q wave in the praecordial lead employed, particularly so in respect of the left oblique position. This is illustrated in Fig. 1 with an example from a patient with an infarction

localized to the anterior wall, where the ECG recordings were carried out via lead V_3 .

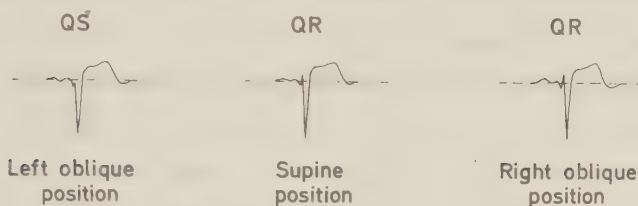


Fig. 1. The influence of posture on the configuration of the QRS complex. The electrode placement corresponds to V_3 in a patient suffering from anterior AMI.

In the supine and right oblique positions, small Q and R waves were measured but when the patient was placed in the left oblique position the R waves became embryonic and indefinable by disappearing below the base line, and as a result, the Q wave was registered as a QS wave having a relatively large amplitude.

Comments

This study has shown that in the set-up employed, measurement of the electrocardiographic components can be carried out with considerable precision, as the error-of-measurement was equal to coefficients of variation between 4 - 7% when using a single praecordial unipolar lead. Several reasons for this should be stressed: 1) the use of the same adhesive silver/silver chloride skin surface electrode throughout the whole period of investigation in the individual patient minimizes the

noise in the electric signal, a) because the silver/silver chloride electrode is very stable, b) because the adhesive type reduces movement artifact and c) because the same permanently attached electrode will reduce the contact impedance due to the electrolyte solution within the electrode (Lewes 1965, Cromwell et al. 1973, Jacobson and Webster 1977). 2) The use of the Mingograph, which is a jet ink-writing electrocardiograph with a very high frequency response, gives excellent registration of the higher frequency components of the QRS, which is of particular value in AMI (Lepeschkin 1963, Jacobson and Webster 1977). 3) The use of a ground cable from the patient to the ECG-instrument, which is connected to good earthy ground, as well as the use of shielded cables, and the avoidance of cable coiling at the input side presumably reduce the capacitive and inductive interference (Blackburn 1965). 4) The use of an electric measuring table (digitizer) to measure amplitudes and deviations of the electrocardiographic components results in good precision (I). 5) Identification of the electrocardiographic components using the Minnesota code criteria prior to measurement on the measuring table gave very low intra-observer and inter-observer variations. 6) The use of the average of 3 consecutive ECG-complexes will smooth out the beat-to-beat variation and the possible effect of any electrical noise (Blackburn 1965, Fischmann et al. 1968).

7) Finally, the measurement of ST segment deviations 60 msec after the last nadir of the QRS complex gives greater precision, as it has been shown that measurement of the deviation 31-60 msec after the nadir of the S wave produces the least variance (Bruce et al. 1966). The latter authors also point out that because of physiologic variations in the diastolic intervals with tachycardia, establishment of a theoretical isoelectric base line from which to measure ST segment shifts necessitates the use of PQ rather than TP intervals.

The biological (background) noise, which includes the method noise (error-of-measurement) in the electrocardiographic components was in the present study expressed by the intra-individual variation of these components in the control patients. The maximum permissible intra-individual variation of these was of the same magnitude as the corresponding variation in another investigation, where this was calculated as the day-to-day variation of patients suffering from conditions considered unlikely to affect the cardiovascular system (Michaels and Cadoret 1967). The ST segment deviation here equalled 0.3 mm and 0.2 mm in V_3 and aVF, respectively, the Q amplitude 0.2 mm in aVF, and the R amplitude 2.4 mm and 1.0 mm in V_3 and aVF, respectively; the Q amplitude in V_3 was not stated, as is the case in the present study. It is quite true that there are no absolute criteria for judging whether a given electrocardiographic item is or is not satisfactory (Simonson et al. 1949), but the

relatively low intra-individual noise of the electrocardiographic components in the present study must be considered as good reproducibility of the measurements using a single surface lead.

A change in the position of the patient, and with this an alteration in the orientation of the heart, results in a measuring error corresponding approximately to the background noise, with the exception of the Q wave in the praecordial lead, where the measuring error was far more pronounced.

It has been shown, using one praecordial lead, that the deviation of the ST segment was independent of the phase of respiration during both relaxed and deep respiration. Further, the amplitude of the QRS complex (R plus S waves) was independent of the respiratory phase during relaxed respiration, but varied considerably with deep respiration (Jobin et al. 1976).

It should therefore be pointed out that during serial electrocardiography using praecordial leads, the recordings must be carried out with the patient in the same well-defined position while breathing in a relaxed manner. In addition, the recordings should be performed on patients at rest, as exercise influences the height of the R wave (Bonoris et al. 1978).

The variability of ST segment, Q and R waves.

The variability of the electrocardiographic

components can be characterized by an inter-individual variation, an intra-individual variation and an error-of-measurement variation (Simonson et al. 1949). The error-of-measurements and the intra-individual variations of these components in control patients were analyzed using pooled standard deviations in the foregoing section. The intra-individual variation and inter-individual variation of the mentioned components will be evaluated in the following by means of analysis of variance. This permits the variance of these components in both infarction and control patients to be mutually related.

A one-way analysis of variance was carried out on the values obtained at the hourly measurements of the electrocardiographic components in the two patient categories, i.e. in AMI patients on measurements within 48 hours and in control patients on measurements within 24 hours; in this manner a number of variance ratios were obtained, the significance of these are shown in Table IVa.

Table IVa. One-way analysis of variance performed on the four patient groups (anterior AMI 14, inferior AMI 16, controls recorded via V_3 15 and via aVF 10 patients), according to ST deviation, Q and R amplitudes.

Groups	Leads	Significance (P)		
		ST deviation	Q amplitude	R amplitude
AMI	Prae-cordial	< 0.001	< 0.001	< 0.001
	aVF	< 0.001	< 0.001	< 0.001
Control	V_3	< 0.001	-	< 0.001
	aVF	< 0.001	< 0.001	< 0.001

It can be seen that in both patient groups, and in both leads, there was a highly significant inter-individual variation of ST segment deviations and amplitudes of Q and R waves. As mentioned earlier, there were no Q waves in lead V_3 of the control patients.

The variances of ST deviation, Q and R amplitudes, respectively, in the group with AMI were related to the corresponding variances in the control group (Table IVb). It was found that the inter-individual

Table IVb. The variances of ST deviation, Q and R amplitudes in patients with anterior and inferior AMI, respectively, related to the corresponding variances in the controls. (Variances from table IVa).

Sources of variance	Leads	Significance (P)		
		ST deviation	Q amplitude	R amplitude
Between individuals	Prae-cordial	< 0.01	-	< 0.05*
	aVF	n.s.	< 0.01	n.s.
Within individuals	Prae-cordial	< 0.001	-	< 0.001*
	aVF	< 0.001	< 0.001	< 0.001

*inverse variance ratio

variations of ST deviation in the praecordial lead and the Q amplitude in lead aVF of AMI patients were significantly greater than the corresponding variations of the control group. There was no difference in the inter-individual variations of the ST deviation and R wave amplitude in aVF between the two groups. Surprisingly, the inter-individual variation of the R wave in the praecordial lead of the control group was significantly greater than that of the AMI

group. However, R waves were only registered in 6 of the patients with anterior AMI during the period under study.

The intra-individual variation in respect of ST deviation in both leads and the Q and R amplitudes in lead aVF were significantly greater in the AMI group than in the control group. However, the reverse was the case with regards to the R wave in the praecordial lead. The latter finding was based on a large number of observations, namely 411 R wave measurements in 15 control patients and 216 measurements in 6 of the 14 patients with anterior AMI.

Comments

There are apparently very few studies on the variability of the electrocardiographic components and these are difficult to compare due to the use of various measuring and analytical techniques. Knowledge of the intra-individual variability is essential for the effective use of serial electrocardiography (Simonson et al. 1949). Thus, the development of an infarction probably produces greater alterations in the ECG than the changes brought about by the intra-individual variability of normal persons, despite this, minor changes are often interpreted as improvement or deterioration in the condition of an AMI patient without exact cognition of the ubiquitous biological (background) noise.

The present investigation showed that the intra-individual variation of the ST segment as well as

of the Q and R waves within 48 hours after the onset of the infarction following hourly recordings in lead aVF, were significantly larger than the corresponding intra-individual variations of the control group. In other words, there was a good signal to noise ratio in this lead, and for this reason lead aVF is preferable for registration of the development of an inferior infarction.

When using the praecordial lead in anterior AMI, the intra-individual variation of the ST segment was significantly greater, and that of the R wave significantly smaller, than the corresponding variation in the control group. Measurement of the ST elevation and the R amplitude in the praecordial lead having the highest initial ST elevation thus gave a good signal to noise ratio with regard to ST segment, whereas it produced an unsatisfactory signal to noise ratio in respect of the R wave. Thus it is advisable to use this lead only for the detection of ischaemic episodes in cases of anterior AMI, but not for evaluation of non-viable myocardial tissue.

It has been demonstrated clinically that the ECG components may be influenced by age, sex, race, body height, body weight and chest configuration (Ishikawa 1976). This is in all probability the reason why a significant inter-individual variation of the electrocardiographic components was found in control patients in the present investigation.

It is not surprising that patients with AMI also have a significant inter-individual variation of these

components, as they have additional events influencing the ECG, i.e. the infarction. As previously mentioned a number of non-ischaemic factors such as drugs, electrolyte disturbances, ventricular conduction defects and pericarditis can also influence the configuration of the ECG (Goldberger 1975, Braunwald and Maroko 1976, Ross 1976, Holland and Arnsdorff 1977). In addition, factors other than infarction can cause ST elevation e.g. Prinzmetal's variant angina and ventricular aneurysm (Prinzmetal et al. 1959, Goldman 1976). In the present study, however, such factors or conditions were excluded and therefore cannot have contributed to the magnitude of the variability (I).

In patients with anterior AMI, the inter-individual variation of the ST segment and R wave in the praecordial lead were significantly greater, respectively smaller than the corresponding variations of the control group. In respect of the ST segment, this finding reflects not only a good signal to noise ratio in the lead, but presumably also that the patients were in various phases of ischaemia. The reason for the latter is that the measurements were commenced at varying times after the onset of AMI (I); further that in all probability, an actual difference between the patients does exist in the severity of the ischaemia. With regard to the R wave, these results can be explained by the poor signal to noise ratio in the lead, and in addition, by the fact that the R wave disappeared in the majority of the patient with anterior AMI during the measurements.

In patients with inferior AMI, using lead aVF, the inter-individual variation of the Q wave was significantly greater than that of the control group, and the inter-individual variation of the ST segment and R wave were of the same magnitude as the corresponding variations of the control group. Why the inter-individual variation of the Q wave was so pronounced in AMI patients is obscure, as there was a good signal to noise ratio for all three components in this lead. However, the fact that the Q wave was registered both as a Q wave per se and at other times as a QS wave may have played a role in this context.

The inter-individual variability must be borne in mind when planning controlled clinical trials, where the intention is to use electrocardiographic components as indicators of the evolution of the infarction. A considerable inter-individual variation as seen in the Q wave will necessitate the inclusion of a larger number of patients, while a smaller inter-individual variation as is the case with the ST segment and R wave will, only require smaller samples for comparison between two or more groups.

The evolution of ST segment, Q and R waves in inferior AMI.

As the most pronounced development of the infarction in man takes place within the first 24 hours after the onset of symptoms (Askenazi et al. 1977, Henning et al. 1978, Selwyn et al. 1978b, Zmyslinski et al. 1979),

it is essential to know the exact time sequence of the ECG changes in the early phase of AMI. In order to achieve this it is necessary that the patients are examined as early as possible after the onset of the symptoms. When analyzing the patient material it was found that the first measurements of the electrocardiographic components were carried out on average 357 minutes after the onset of the symptoms in patients with anterior AMI and on average after 155 minutes in those with inferior AMI (I). The latter were therefore selected to comprise the material for studying the spontaneous evolution of the ST segment, Q and R waves. Furthermore, 4 hours was chosen arbitrarily as the latest time at which the first ECG had to be recorded, in this manner the group consisted of 14 patients (II).

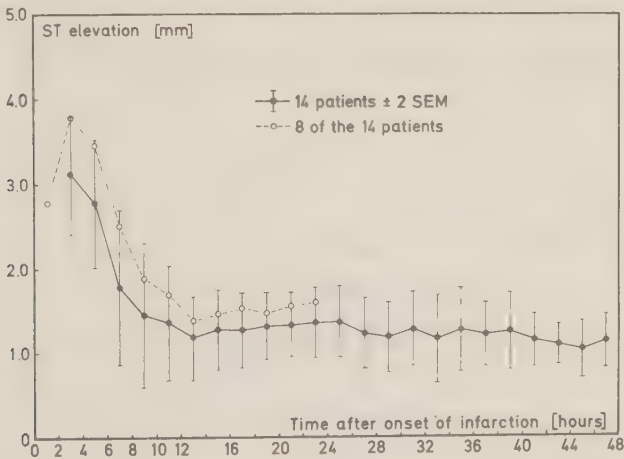


Fig. 2. Mean ST elevation at intervals of 2 hours from the onset of symptoms of AMI (aVF lead).

Fig. 2 shows that the highest average ST elevation was measured in the 2-4 hour interval. Thereafter it decreased to a stable level at the 12-14 hour interval.

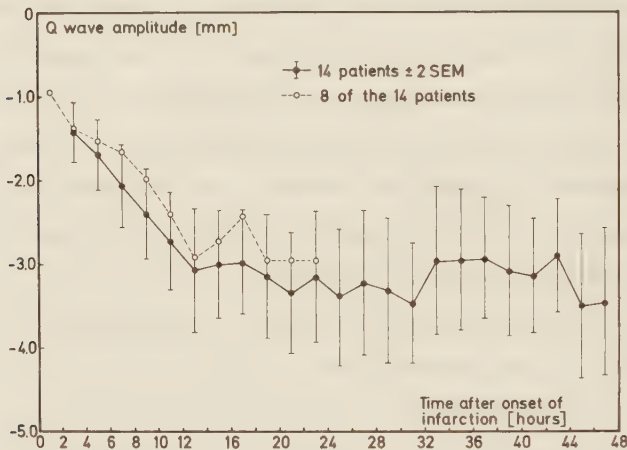


Fig. 3. Mean amplitude of Q wave at intervals of 2 hours from the onset of symptoms of AMI (aVF lead).

In fig. 3 the average amplitude of the Q wave increased almost linearly from the 0-2 hour to the 12-14 hour interval. The amplitude became somewhat erratic in the following period.

Fig. 4. shows the average amplitude of the R wave decreased almost linearly from the 2-4 to the 14-16 hour intervals. Thereafter it was at a fairly uniform level.

A considerable scatter of the curves was present in figures 2, 3 and 4, reflecting the pronounced inter-individual variation of the electrocardiographic components.

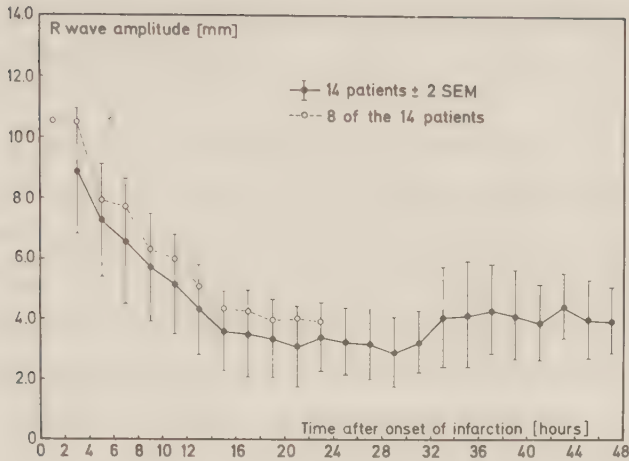


Fig. 4. Mean amplitude of R wave at intervals of 2 hours from the onset of symptoms of AMI (aVF lead).

There was not only a significant positive linear correlation ($r = 0.95$, $P < 0.001$; $r^2 = 0.90$) between the average amplitudes of the Q and R waves within 48 hours after the onset of the infarction, but also between the individual amplitudes of these in 13 of the 14 patients (II).

As shown in Table V the ST segment elevation at 2-4 hours (average ST elevation between 121 and 240 minutes) of each patient was correlated to ΔQ and ΔR , respectively. These Δ values, which were presumed to indicate the fully developed QR changes, were calculated as the difference between the measured amplitudes at 2-4 hours (121-240 minutes) and at 23-25 hours (1381-1500 minutes). One of the 14 patients was not included in the

analysis due to QRS prolongation at 24 hours. ST elevation at 2-4 hours was significantly positively correlated to ΔR ($r = 0.57$, $P < 0.05$), but not to ΔQ or $\Delta(Q+R)$.

Blood samples were withdrawn at 3 to 4 hourly intervals for the first 48 hours after admission and then 3-4 times daily for approximately one week (Hørder et al. 1981). These were used for the calculation of the appearance function (AF) of CK in plasma, based on a two-compartment model, as described elsewhere (Petersen et al. 1981). The cumulated appearance function of CK in plasma ($CK-AF_{cum}$) which can be employed as a reasonable estimate of infarct size (Hørder et al. 1981, Petersen et al. 1981), was correlated to ΔQ , ΔR and $\Delta(Q+R)$ as seen in table V. $CK-AF_{cum}$ was significantly positively

Table V. ST elevation at 2-4 hours and AF_{cum} of CK correlated to ΔQ , ΔR and $\Delta(Q+R)$, respectively, in patients suffering from inferior infarction using lead aVF.

	Coefficients of correlation		
	ΔQ	ΔR	$\Delta(Q+R)$
ST elev. at 2-4 hours	- 0.23	0.57	0.54
AF_{cum} of CK	0.14	0.62	0.80

AF_{cum} of CK = cumulated appearance function of CK in plasma
 ΔQ = Q amplitude at 2-4 hours - Q amplitude at 23-25 hours
 ΔR = R amplitude at 2-4 hours - R amplitude at 23-25 hours

correlated to ΔR ($r = 0.62$, $P < 0.05$) and $\Delta(Q+R)$ ($r = 0.80$, $P < 0.001$) but not to ΔQ . Finally it was shown that

the ST elevation at 2-4 hours was significantly positively correlated to $CK-AF_{cum}$ ($r = 0.58$, $P < 0.05$).

Comments

Previous studies have demonstrated that lead aVF is the most suitable lead in clinical ECG recordings for the recognition of inferior wall infarction (Myers et al. 1949, Goldman 1976); the present investigation has, in addition, shown that this lead is reliable for monitoring the evolution of such an infarction.

The average maximum ST segment elevation occurred 2-4 hours after the onset of the infarction and decreased thereafter to a uniform level within the period 12-48 hours. Approximately the same results have been achieved in other investigations (Selwyn et al. 1978b).

The Q and R waves started to develop shortly after the infarction (within 4 hours) and progressed rapidly within 12-16 hours, after which they flattened out. Almost similar observations were made by Selwyn et al. (1978b). Whether the Q and R waves are fully developed within the first 48 hours after infarction cannot be determined from the present study.

Within 48 hours after the occurrence of inferior infarction a highly significant positive correlation was observed between the average amplitude of the Q and R waves; expressed in another manner, 90% of the variation in the amplitude in one of the waves could

be explained from the amplitude of the other. This would appear to indicate that they are equally good in lead aVF for monitoring transmural inferior infarction.

As mentioned in Chapter I, considerable effort has been expended on the development of enzyme models permitting the quantitative assessment of infarct size. It has thus been reported that calculation of the appearance of enzymes in plasma, based on a two compartment distribution model provides a meaningful estimation of the release of enzymes by the myocardium (Hørder et al. 1981, Petersen et al. 1981). Employing this model, the cumulative appearance function of CK in plasma has been used in the present study as a valid estimate of infarct size.

There appears to be little doubt regarding a correlation between changes in the QRS complex and the extent of the myocardial infarction, as described in Chapter II. In the present study very variable relationships were found between the development of various amplitudes of the QRS complex and the infarct size as determined by enzyme analysis. Thus, $CK-AF_{cum}$ was closely correlated to $\Delta(Q+R)$, weakly correlated to ΔR , while no correlation existed to ΔQ . Consequently, it seems reasonable to assume that $\Delta(Q+R)$ is the best ECG-estimate of infarct size.

The feasibility of predicting the extent of the completed myocardial infarction from the early ST elevation has attracted considerable interest. This study

has shown that the correlation between the ST elevation during the 2-4 hour interval and $CK-AF_{cum}$ was relatively weak. The correlation between ST elevation at that time and ΔR and $\Delta(Q+R)$, respectively, were also weak, and with regard to ΔQ there was no correlation at all. The latter agrees with another investigation in which no relation was found between maximum ST elevation and maximum Q amplitudes in leads II + III + aVF (Yusuf et al. 1979a). Thus, the prediction of complete QRS changes, as well as the infarct size, in lead aVF in cases of inferior infarction from the early ST elevation is of limited value.

The correlation between ST elevation and clinical parametres.

It would be reasonable to presume that the pronounced variability of the ST segment in the early phase of AMI could be due to a corresponding variability in the clinical parametres, as these influence, or could have some connection with, the myocardial ischaemia, for instance heart rate, blood pressure, respiratory rate, oxygen treatment and retrosternal pain (I).

Using a single surface lead, the ST elevations were measured hourly within the first 48 hours after the onset of symptoms and related in both AMI groups to clinical variables (I). Thus, correlation coefficients were obtained for each patient, for heart rate, mean arterial blood pressure, the product of heart rate and systolic blood pressure, and respiratory rate. The distributions of

the coefficients of correlation after Fisher's z -transformation were evaluated by means of a χ^2 -distribution (Snedecor and Cochran 1969, Documenta Geigy 1975). It was found that there was a highly significant dispersion of the correlation coefficients within the groups (I).

The presence of retrosternal pain was registered, based on information supplied by the patients. Comparisons were made with the paired t -test between the measured ST elevation in patients with anterior AMI, partly before and after the pain commenced and partly before and after the pain ceased. In neither case was it possible to demonstrate that the pain had any influence on the ST elevation (I).

Patients with anterior AMI were studied for the influence of nasal oxygen therapy (flow of 2-6 min/l) on ST elevation. A comparison between the measured ST elevation before and after the administration of oxygen and before and after the cessation of oxygen therapy, respectively, showed that oxygen treatment had no influence on the ST elevation (I).

Comments

Arterial hypoxaemia is common during the first few days after AMI (Valencia and Burges 1969, Sukumalchantra et al. 1970, Brest 1975, Nielsen 1975), and it has been demonstrated experimentally that hypoxaemia

increases the ischaemic injury after coronary occlusion (Radvany et al. 1975). It has been reported that following acute coronary ligation, the administration of 40% and 100% inspired oxygen decreases acute ischaemic injury as measured by epicardial ST segment mapping and myocardial CK (Maroko et al. 1975). However, in another study, 40% oxygen administered prior to coronary occlusion did not prevent an increase in the epicardial ST segment (Bodenheimer et al. 1978), and following the use of thermography to study the changes in the infarct size, it was found that 100% oxygen does not appear to have a favourable effect on an experimentally induced acute myocardial infarction (Malm et al. 1977). A difference in the measuring techniques is the probable cause of the conflicting results regarding the influence of oxygen on the ischaemic damage. On the other hand, it has been postulated, that a high concentration of oxygen promotes a lowering of the coronary artery perfusion pressure, and in addition, it may somehow decrease the arterial supply from the vascular bed round the ischaemic area (Malm et al. 1977). Diverging results have also been observed in human AMI. Thus, it has been found that enrichment of inspired oxygen content reduced ST elevation as recorded in praecordial mapping (Madias et al. 1976). In the present study, however, nasal oxygen therapy had no influence on the ST elevation in patients with anterior AMI. It is possible that the administration of an oxygen flow

of 2-6 l/min is too low to influence myocardial ischaemia; further, that the use of a single praecordial lead is a technique which is too insensitive to trace an eventual effect of oxygen therapy on the ischaemia.

Using praecordial ECG-mapping or vectorcardiography, it has been shown that attacks of cardiac pain result in an increased ST elevation (Maroko et al. 1972, Madias et al. 1975, Kronenberg et al. 1976). However, in the present study with the use of a single praecordial lead, the commencement and cessation of chest pain had no influence on the hourly measured ST elevations in patients with AMI. However, little weight should be laid upon this aspect of the study due to the fact that the general impression gained was that the threshold of pain varied considerably. Another point is that the employed lead may be too insensitive to follow ST changes caused by ischaemic pain.

The fact that increased heart rate also increases ischaemic damage has been demonstrated in experimental studies (Maroko et al. 1971, Redwood et al. 1972). Similar observations have been described in case reports (Richman 1974, Madias 1977). In this study, a significant positive correlation could only be demonstrated between ST elevation and heart rate in a few patients. This was perhaps due to the fact that the heart rate in the majority of patients was within the normal range, where

changes in myocardial oxygen consumption are possibly too small to cause any significant alteration of the ST segment.

A reduction in arterial blood pressure decreases myocardial wall tension and lowers myocardial oxygen requirements. If there is a concomitant severe decrease in coronary perfusion pressure, there is a tendency for the myocardial oxygen delivery to the ischaemic area to be diminished also. This will thus interfere with the beneficial effect on ischaemia obtained from the decrease in myocardial oxygen requirement (Maroko et al. 1971, Redwood et al. 1972). These two contrary effects of lowering the arterial blood pressure can possibly be the cause of why this investigation was unable to demonstrate any pattern of the coefficients of correlation between ST elevation and mean arterial blood pressure.

The product of heart rate and systolic blood pressure has been employed clinically as a reasonable indirect measure of the oxygen consumption of the myocardium (Kitamura et al. 1972). In patients with AMI, a rising product should thus result in a rising ST elevation, but no such relationship could be demonstrated in the present study.

When pulmonary disease can be excluded in patients with AMI, increased respiratory rate usually indicates the presence of cardiac insufficiency, which is normally related to the extent of the injured myocardium

(Master et al. 1937, Brest 1975). In the present investigation, 93% of the patients had congestive heart failure; despite this, only 36% of the patients with anterior AMI had a positive correlation between respiratory rate and ST elevation; in patients with inferior AMI, there was no positive correlation at all between these variables.

As there was a significant dispersion of the coefficients of correlation within the individual groups in which a correlation was made between ST elevation and heart rate, mean arterial blood pressure, heart rate multiplied by systolic blood pressure, and respiratory rate, respectively, it must be emphasized that the variability of the ST elevations was most often inexplicable and only rarely attributable to alterations in the clinical status. There can be several causes of this inconstant correlation, which reflects the previously mentioned pronounced inter-individual variation. On the one hand, it is possible that the clinical variables are poorly correlated to myocardial ischaemia when these variables mainly lie within normal ranges; this is in contrast to experimental conditions where the heart rate and blood pressure are artificially provoked to extreme values (Maroko et al. 1971, Redwood et al. 1972) with a subsequent greater influence on myocardial oxygen consumption. On the other hand, as earlier mentioned, factors other than ischaemia may effect the ST segment. Thirdly, it may be of importance for the inconstant

correlation that patients were included in the study at different times after the onset of chest pain. Finally, it must be assumed that the use of a single lead is an insufficient method when studying changes of the ST segment as a result of changes in clinical variables.

The application and limitation of a single surface lead.

ECG-recording via a single surface unipolar lead is a simple non-invasive method, which is rapid and easily employed, and causes no discomfort to the patients. The measurement of the electrocardiographic components by means of an electric unit connected to a desk computer was rapid and precise.

In the lead aVF there was, in patients with inferior AMI, an optimal signal to noise ratio of all three electrocardiographic components, and, in addition, $\Delta(Q+R)$ appears to be a reasonable ECG-estimate of infarct size. For these reasons this lead is recommendable for following the evolution of an inferior infarction. However, the predictability of the complete QRS changes as well as the infarct size from the early ST elevation was of limited utility in lead aVF.

In the praecordial lead initially having the highest ST elevation in cases of anterior AMI, there was a good signal to noise ratio with regard to the ST segment,

but not in respect of the R wave; this could not be ascertained for the Q wave; on the other hand, the Q wave was very sensitive to changes in the heart position. The spontaneous development of an anterior infarction should therefore not be studied in a single praecordial lead, but instead more praecordial leads should be used as shown in the next chapter.

The greatest disadvantage of the electrocardiographic method for monitoring infarctions is its restriction to patients free of non-ischaemic factors significantly influencing the ECG components.

CHAPTER IV

The use of praecordial ECG-mapping.

Study groups.

Sixteen patients with anterior AMI, whose initial ECG recording showed a ST elevation ≥ 2 mm in one or more of the leads $V_1 - V_6$, and whose first ECG-map was recorded ≤ 4 hours after the onset of symptoms (i.e. retrosternal pain of more than 20 min duration) were examined. Other inclusion criteria were similar to those in Chapter III. The patients were admitted to the CCU on average 2 hours (range 0-3) after the infarction. Their average age was 59 years (range 40-77), 13 were men and 3 women. As earlier, the diagnosis was established using WHO criteria: all the patients developed signs of infarction on the routine ECG recording, and, in addition, a diagnostic rise in the routinely determined serum enzymes CK, ASAT and LD (Working group 1971). All were suffering from their first transmural AMI.

The treatment in the CCU has been described earlier. Four patients were treated during the period of observation with digoxin from the 3rd to 4th days after admission and one patient was treated with a beta-adrenergic blocking drug from the 7th day. Based on Killip and Kimball's

classification of heart failure in AMI (1967) 13 developed mild to moderate heart failure and 3 patients pulmonary oedema. Two died during admission, one on the 14th and the other on the 30th day (III and IV).

The control group comprised 10 patients admitted to the CCU due to chest pain, but without AMI (III). Their average age was 54 years (range 30-71], 7 were men and 3 women. The patients of both groups gave their informed consent.

Comments

In the study using a single lead in cases of inferior AMI, it was found, that the most pronounced ECG alterations occurred early after the onset of symptoms. Therefore, it was essential when designing a study of ECG changes in anterior infarctions using ECG-mapping to examine the patients as early as possible. Consequently, the present investigation was confined to patients where the first ECG-map was recorded within 4 hours after the onset of infarction.

Both the AMI group and the control group consisted of patients whose age and sex distribution was similar to those earlier reported from this CCU (Nielsen 1970, 1973, Thygesen et al. 1974, Nielsen 1975, Thygesen et al. 1977). The frequency of congestive heart failure was high in the present material whereas that

of cardiogenic shock and the mortality were low, as compared to the above mentioned series (see Chapter III).

The method.

The signals from 42 unipolar praecordial leads were registered via shielded cables on an Elema-Schönander Mingograph 81, using a flexible synthetic plate (45 x 20 x 0.2 cm), in which were positioned 42 silver/silver chloride electrodes, floating type, in 6 horizontal and 7 vertical rows.

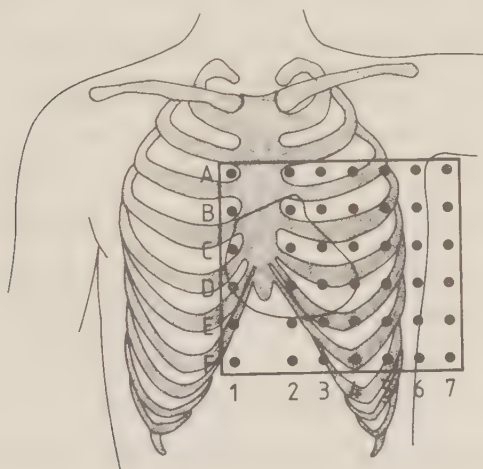


Fig. 5. The position of the praecordial ECG-map.

The distance between the horizontal rows was 3 cm and the plate was placed so that row A lay above the second

intercostal space at the sternum (Fig. 5). Holes had been drilled at 1.5 cm intervals thus permitting the electrodes to be moved so that the vertical rows could fit the individual chest. Rows 1 and 2 were placed along the right and left sternal borders, respectively, and rows 6 and 7 along the left anterior and middle axillary lines, respectively. Rows 3, 4 and 5 were determined by dividing the distance from rows 2 to 6 by 4. Correct replacement of the synthetic plate at later mappings was ensured by marking the edges of the plate on the chest wall. The electrodes were mounted on ball joints at the end of plastic rods, which fitted into holes in the synthetic plate and which could be fastened by means of a nut. A spring was inserted around the rod, between the plate and ball joint. This construction, together with the flexibility of the plate and a slight pressure permitted all 42 electrodes to be in contact with the skin during the recording, irrespective of the form and contour of the thorax. During the pilot phase, the synthetic plate was attached to the thorax by means of a belt. However, experience showed that slight pressure exerted on the plate was better and more practical, as all the electrodes were then definitely in contact with the chest, without any discomfort to the patient. A jelly was applied to the electrodes prior to ECG recording (mapping); this was removed again using warm water. An electric lead selector (Siemens) was

mounted on the 6 channel electrocardiograph. The former was constructed so that the signals from the 42 leads were automatically recorded in 7 sequences (III). A reset function was introduced between each sequence in order to counteract base-line drift. The paper speed was 50 mm per sec and the calibration 1 mV = 10 mm. The ECG-mapping was carried out with the patient in the supine position with a 30° elevation of the upper part of the bed. The duration of each mapping was 1 to 2 minutes.

As earlier, the ECG complexes were analyzed by means of a Hewlett-Packard 9864A digitizer/9810A calculator. The criteria employed were similar to those given in Chapter III, with the exception that the ST segment was measured 20 msec after the J point. Measurement of the complexes in an ECG-map and transfer of these data to punch cards for electronic data processing took approximately 30 minutes. Praecordial maps were excluded if the average QRS duration in a map was ≥ 120 msec, or if a definite change occurred in the QRS frontal plane axis in two consecutive maps.

ΣQ , ΣR and ΣST were calculated for each ECG-map, NST only in the AMI group. ΣQ equals the sum of the amplitudes of the Q (QS) waves. ΣR equals the sum of the R wave amplitudes. In the control patients ΣST equals the sum of the ST elevation in the leads where the deviations were > 0 mm. In the patients with infarction,

NST equals the number of leads with ST elevation ≥ 1.5 mm, while Σ ST equals the sum of the ST elevations in these leads (III and IV).

Comments

The experimental and clinical basis for the use of praecordial ECG were presented approximately 35 years ago (Wilson et al. 1944). These authors described the ECG changes occurring after AMI; which were later definitely established by extensive post mortem studies (Myers et al. 1948a-b, 1949a). Following the introduction of body surface electrocardiographic mapping, using up to 240 leads, it became possible to obtain information of regional cardiac events not detected by conventional ECG recordings (Taccardi 1963, Abildskov et al. 1977). A special version of the mapping technique having fewer praecordial leads was developed while trying to find a method suitable for sizing myocardial ischaemic lesions. This, so-called, praecordial ECG-mapping has been established in many centres, however, at present the technique varies so much that each group of investigators can be identified by the number or type of electrocardiographic leads employed (Muller et al. 1978). Thus, investigations have been reported using 72 leads (Reid et al. 1971, Selwyn and Shillingford 1977), 49 leads (Madias et al. 1975, Horgan et al. 1980), 48 leads (Reid et al.

1974, Flaherty et al. 1976, Essen et al. 1977), 42 leads (Thompson and Katavatis 1976), 39 leads (Inoue et al. 1979), 35 leads (Maroko et al. 1972, Akiyama et al. 1975, Awan et al. 1976, Jobin et al. 1976, Norris et al. 1976, Luxton et al. 1977, Hardarson et al. 1978, Jugdutt and Lee 1978, Yusuf et al. 1979a), 24 leads (Herlitz and Hjalmarson 1979) and 18 leads (Bussman et al. 1979). On the one hand, it has been postulated that since improvement in the method is required this pluralistic approach is desirable and likely to promote development (Muller et al. 1978), but on the other hand, it has been suggested that a standardization of the number of leads is desirable (Schoffa and Schaefer 1978).

While measurement of the deviation of the ST segment 60 msec after a reference point within the QRS complex was feasible when using only one lead (I) it was unsuitable in a map. The reason being that the configuration of the 42 QRS complexes was non-uniform, thus giving different reference points for measurement of the ST elevation. It was decided instead to measure the ST deviation 20 msec after the J point, which approximately corresponds to the interval 31-60 msec after the nadir of the S wave, as recommended by Bruce et al. (1966). This procedure has also been employed in other studies (Akiyama et al. 1975, Muller et al. 1975, Hardarson et al. 1978).

In praecordial ST segment mapping, the sum of all ST segment elevations (Σ ST) has been taken as an

index of the magnitude of the ischaemic damage, and the number of leads showing ST segment elevation (NST) above a certain level has been taken as an index of the extent of the ischaemic injury (Maroko et al. 1972). Different criteria for the deviation of the ST segment have been reported when calculating NST: All leads with a ST elevation of 0.5 mm or greater (Thompson and Katavatis 1976, Inoue et al. 1979), greater than or equal to 1 mm (Maroko et al. 1972, Akiyama et al. 1975, Awan et al. 1976, Jobin et al. 1976, Madias et al. 1976, Hardarson et al. 1978, Yusuf et al. 1979a, Horgan et al. 1980), greater than or equal to 2 mm (Pelides et al. 1972, Merx et al. 1977, Selwyn et al. 1978c, Yusuf et al. 1979a). However, it was found that 1 mm, 1.5 mm and 2 mm used as the criteria for ST deviation were all equally appropriate (III). A border limit of 1.5 mm was employed in the present study because the correlation between NST and heart rate, using this figure produced the highest mean coefficient of correlation (III). In patients with AMI, the same criterion for ST deviation was used when calculating both Σ ST and NST in this investigation. This has been employed by others also (Pelides et al. 1972, Awan et al. 1976, Jobin et al. 1976, Horgan et al. 1980). However, in the majority of reports Σ ST has been calculated as the sum of all the leads with elevation (Maroko et al. 1972, Reid et al. 1974, Akiyama et al. 1975, Muller et al.

1975, Flaherty et al. 1976, Madias et al. 1976, Thompson and Katavatis 1976, Merx et al. 1977, Hardarson et al. 1978, Jugdutt and Lee, 1978, Bussmann et al. 1979, Inoue et al. 1979, Yusuf et al. 1979a, Horgan et al. 1980). The same procedure was used in the present study in patients without AMI. In other investigations the Σ ST was calculated as the sum of ST elevation from leads whose elevation was equal to or greater than 1mm (Luxton et al. 1977, Zmyslinski et al. 1979) and 2 mm (Norris et al. 1976, Selwyn et al. 1977a). Finally, the limit of ST elevation ≥ 1.5 mm has been employed to separate the leads considered liable to develop further electrocardiographic changes (Maroko et al. 1977, Muller et al. 1978).

The reliability of the measurements.

Various components of variance, which were included in the error-of-measurement of praecordial ECG-mapping are described in (III). The highest calculated

Table VI. Estimates of error-of-measurement variation, day-to-day variation and patient position variation in ECG-mapping. The estimates are expressed as PSD, each based on ten replicates.

	Pooled standard deviation (mm)		
	Error-of-measurement variation	Day-to-day variation	Patient position variation
Σ ST elevation	4.09	6.82	4.99
Σ Q amplitude	2.78	23.00	37.55
Σ R amplitude	18.32	44.55	48.79

PSD's of these were employed as an estimate of the error-of-measurement of the method (Table VI); expressed as coefficient of variation, $\Sigma ST = 3.5\%$, $\Sigma Q = 1.5\%$ and $\Sigma R = 4.5\%$.

The calculated PSD's for the day-to-day variation as shown in table VI were used as the estimate of the intra-individual variation of the control patients; These include the error-of-measurement of the method. The upper limit of normal day-to-day variations were, as earlier, based on 95 per cent confidence interval and termed maximal permissible day-to-day or intra-individual variation (Michaels and Cadoret 1967). Calculated by means of the one-tailed test of the t-distribution, these were on measurement of ΣST elevation 12.5 mm, of ΣQ amplitude 42.2 mm and of ΣR amplitude 81.7 mm.

No significant difference could be demonstrated when the estimates for the intra-individual variation ($\Sigma ST = 6.82$ mm, $\Sigma R = 44.55$ mm) were divided by the number of leads employed (i.e. 42) and compared to the corresponding figures for a single praecordial lead (Chapter III). A similar comparison for the Q wave could not be carried out due to the absence of Q waves of the controls when using a single praecordial lead (Chapter III).

Induced measuring errors were brought about by changes in the position of the control patients (III). The highest of the calculated PSD's was used as an estimate of the induced measuring error, as shown in Table VI. It

was found that these PSD's were of the same magnitude as those obtained from the day-to-day variation (= the intra-individual variation), and with regard to ΣST also of the same magnitude as the PSD of the error-of-measurement, whereas for both ΣQ and ΣR , they were significantly greater than the error-of-measurement ($P < 0.001$ and $P < 0.01$, respectively).

Comments

The present investigation demonstrated that measurement of ΣST , ΣQ and ΣR were precise, as the error-of-measurements gave coefficients of variation of 2-5%. The many factors contributing to the excellent precision with a single lead presumably also apply to 42 leads, as the principle of the measuring set-up was identical.

The precision of the ECG-mapping was, in all probability, enhanced due to the design of the synthetic plate and electrode attachment, which ensured good contact with the chest. Further, the use of the floating type of electrode and electrode jelly counteracted any tendency to movement artifact because of the electrolyte bridge formed by the jelly between the metal of the electrode and the skin (Cromwell et al. 1973). Another factor favourably influencing the precision was the use of a specially constructed lead selector, which automatically reset the base-line after each of the 7 sequences.

This resetting was necessary due to the inevitable baseline drift when switching from one vertical line of leads to the next (Lepeschkin 1963).

The biological (background) noise when measuring ΣST , ΣQ and ΣR was expressed by the intra-individual variation (day-to-day variation) of the control patients. In a praecordial map these were of the same magnitude as in a single lead multiplied by 42, i.e. the biological noise oscillates synchronously, irrespective of the number and the placement of the leads. This observation strongly supports the vectorial theory that all body-surface leads record the same electrical forces (Beckwith 1970).

The findings in respect of changes in body position on the electrocardiographic components of a map are in agreement with the results of another investigation using praecordial mapping on patients without AMI in which only the amplitude of the QRS complex varied (Jobin et al. 1976). Previous studies of praecordial mapping have shown not only that a change in posture but also the phase of respiration and exercise must be taken into account when assessing electrocardiographic changes (Selwyn and Shillingford 1977, Selwyn et al. 1977a-b). Therefore, repeated ECG-mapping should be carried out with the patient at rest, with quiet respiration and in the same well-defined position. But should the ECG-mapping

be carried out under less stringent conditions, then the induced measuring error will be within the range of the ever-present biological background noise.

The variability of ΣST , ΣQ and ΣR .

Due to the experience gained in the investigation using a single lead, the present study was planned in such a manner that in addition to determining the individual variability, the time variability could also be established. Consequently all patients were mapped using a set time schedule (4, 6, 8, 12 and 24 hours and thereafter once a day for a week and on day 14) (III).

There was a significant inter-individual variation of ΣST , ΣQ and ΣR both in the AMI and control groups (Table VIIa). There were also significant inter-

Table VIIa. Two-way analysis of variance performed on the two patient groups according to ΣST , ΣQ and ΣR , with cross classification based on individuals and time from onset of infarction.

Groups	Sources of variance	Significance (P)		
		ΣST	ΣQ	ΣR
AMI	Between individuals	< 0.001	< 0.001	< 0.001
	Between periods	< 0.001	< 0.001	< 0.001
Control	Between individuals	< 0.001	< 0.001	< 0.001
	Between periods	< 0.05	n.s.	n.s.

period variations of these in the AMI group and of ΣST in the control patients.

Table VIIb. The variances of ΣST , ΣQ and ΣR in AMI patients related to the corresponding variances in control patients. (Variances from the two-way analysis of variance in Table VIIa).

Sources of variance	Significance (P)		
	ΣST	ΣQ	ΣR
Between individuals	< 0.001	< 0.001	< 0.001
Between periods	< 0.05	< 0.05	< 0.05
Within individuals	< 0.001	< 0.001	n.s.

As shown in table VIIb both the inter-individual variation and the inter-period variation of ΣST , ΣQ and ΣR , respectively, were significantly greater in the group with AMI than in the control group. The intra-individual variation of ΣST and ΣQ were significantly greater in the group with AMI than in the control group; this did not apply to ΣR . However, if only values obtained between 6 and 24 hours after the onset of the infarction were analyzed, then the intra-individual variation of ΣR in the AMI group was also significantly greater than that in the controls ($P < 0.05$).

Comments

The observation that the intra-individual variation of both ΣST and ΣQ were greater in the AMI group

than in the control group reflects a good signal to noise ratio of these in cases of AMI. On the other hand, there was an unsatisfactory signal to noise ratio in respect of ΣR , measured over a period of 14 days, but this was more satisfactory within 6 to 24 hours. The last mentioned period was also that in which the most pronounced changes of ΣR occurred (IV).

The great inter-individual variation of ΣST , ΣQ and ΣR both in patients with and without AMI was similar to the study using a single lead. In Chapter III various possible causes of this variation were mentioned, but in addition to these a number of factors are applicable to the present study. 1) Five patients were given digoxin or a beta-adrenergic blocking drug, and this may have influenced ΣST . 2) As all the patients developed heart failure, it should be borne in mind, that it has been shown on the basis of experimental studies, that the QRS voltage may be influenced by alterations in the end-diastolic volume through the so-called Brody effect (Voukydis 1974). This effect produces an accentuation of electromotive forces oriented radially and an attenuation of the effects of the forces oriented tangentially (Brody 1956). However, this hypothetical model has not been verified in patients suffering from AMI (IV). 3) Secondary changes of ST segment can occur due to prolongation of the QRS complex in cases of local intramyocardial conduction delay as

mentioned in Chapter II. This occurred in fewer than 10% of the electrodes in studies with epicardial mapping (Heng et al. 1976), whereas in human mapping no such figure can be given; among other reasons due to the fact that various definitions have been suggested for the term local intra-myocardial conduction delay (Beckwith 1970, Goldman 1976). Therefore, according to Goldman (1976), only leads showing a QRS duration < 0.12 sec were included in the analysis of predictability; the last-named will be discussed later.

The pronounced time variation of ΣST , ΣQ and ΣR in cases of AMI has also been observed by others (Madias and Hood 1977, Merx et al. 1977, Selwyn and Shillingford 1977, Hardarson et al. 1978, Henning et al. 1978, Zmyslinski et al. 1979).

In contrast to this, time variation was only significant with regard to ΣST in the control group. This instability of ΣST may be rather surprising, but once again factors other than ischaemia also influence the ST segment.

The evolution of ST segment, Q and R waves in anterior AMI.

The spontaneous development of the ST segment as well as that of the Q and R waves within one year of an anterior myocardial infarction were studied by means of praecordial ECG-mapping.

The average course of ΣST decreased from 2 to 8 hours; from 8 to 24 hours it remained at approximately the same level, whereafter there was a significant secondary elevation. This was maximal from days 2 to 5, after which ΣST decreased significantly (Fig. 6).

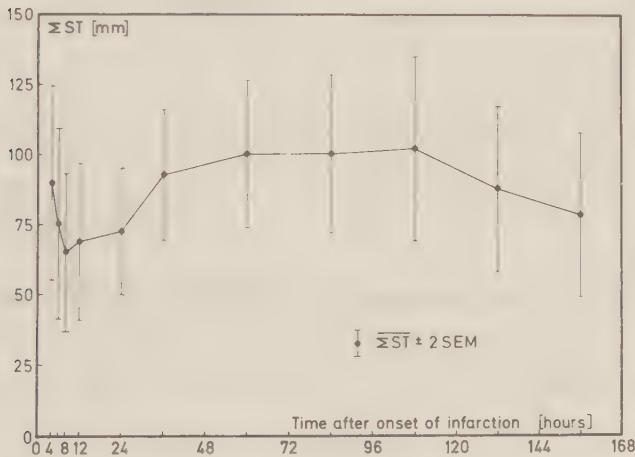


Fig. 6. Mean ΣST elevation throughout one week after anterior AMI.

One year later, ΣST was approximately zero. The average course of NST was similar to that of ΣST . Further, it was found that ST elevation at 4 hours in each lead of the maps was closely correlated to the secondary ST elevation ($\bar{r} = 0.84$, $P < 0.001$) (IV).

The average amplitude of ΣQ began to increase at 3 hours. As shown in Fig. 7 the maximum deflection was

reached on average after 24 hours (range 8-45). A reduction in ΣQ amplitude after one week occurred, so that one year later, it was at the same level as that of 8 hours (IV).

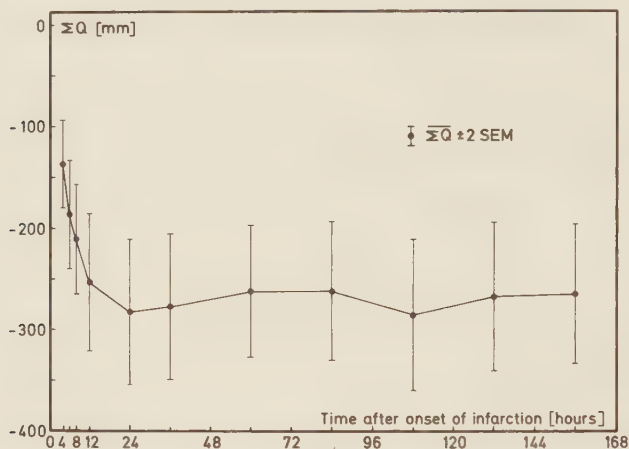


Fig. 7. Mean ΣQ amplitude throughout one week after anterior AMI.

The average ΣR amplitude was decreasing at 2 hours. The maximum rate of decrease took place within 24 hours (range 12-54). From day 14 until one year later, the average ΣR had increased to the same height as at 8 hours (IV).

In figures 6, 7 and 8 there was a considerable scatter of the curves reflecting the great inter-individual variation.

The ST elevation at 4 hours was used as an estimate of the primary ST elevation (ST_{prim}). These were

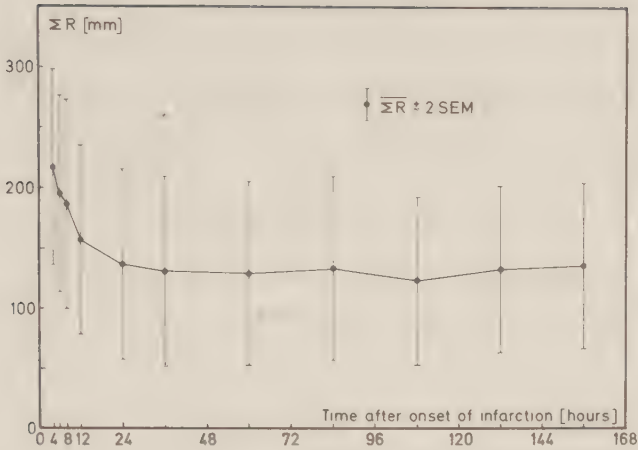


Fig. 8. Mean ΣR amplitude throughout one week after anterior AMI.

employed as they were the earliest measurements available in all the patients except one. ΔQ was calculated as the difference between the Q amplitudes at 4 and 24 hours. ΔR was calculated in a similar manner.

Table VIII. ΣST elevation at 4 hours and AF_{cum} of CK correlated to $\Delta \Sigma Q$, $\Delta \Sigma R$ and $\Delta \Sigma(Q+R)$, respectively, in 15 patients suffering from anterior infarction using ECG-mapping.

	Coefficients of correlation		
	$\Delta \Sigma Q$	$\Delta \Sigma R$	$\Delta \Sigma(Q+R)$
ΣST elevation at 4 hours	0.35	0.52	0.54
AF_{cum} of CK	0.28	0.28	0.35

AF_{cum} of CK = cumulated appearance function of CK in plasma

ΔQ = Q amplitude at 4 hours - Q amplitude at 24 hours.

ΔR = R amplitude at 4 hours - R amplitude at 24 hours

As shown in table VIII the ΣST_{prim} was significantly correlated to $\Delta \Sigma R$ ($P < 0.05$) and $\Delta \Sigma(Q+R)$ ($P < 0.05$), but not to $\Delta \Sigma Q$. As these relatively low coefficients of correlation could have been caused by the previously mentioned considerable inter-individual variation of ΣST , ΣQ and ΣR , a further analysis of correlation was carried out between the electrocardiographic components in respect of each lead of the maps in each patient. It was found that ST_{prim} was significantly correlated to ΔQ ($\bar{r} = 0.48$, $P < 0.001$), and $\Delta(Q+R)$ ($\bar{r} = 0.57$, $P < 0.001$), but not to ΔR ($\bar{r} = 0.12$, n.s.) (IV).

In exactly the same manner as in Chapter III the $CK-AF_{\text{cum}}$ was calculated for each patient. As shown in table VIII, there was no correlation between $CK-AF_{\text{cum}}$ and $\Delta \Sigma Q$, $\Delta \Sigma R$ and $\Delta \Sigma(Q+R)$, respectively; neither was there any correlation between ΣST_{prim} and $CK-AF_{\text{cum}}$ ($r = 0.33$, n.s.).

Comments

Praecordial ST segment elevation develops rapidly after the onset of anterior infarction, and it has been found in studies of praecordial ECG-mapping that ST elevation rises to a maximum within one hour (Selwyn et al. 1977a). Many investigations, including the present, have demonstrated a decrease in ΣST and NST within 8-12 hours (Merx et al. 1977, Hardarson et al.

1978, Rubenstein and Freitas 1978, Essen et al. 1979a, Zmyslinski et al. 1979). A secondary rise in Σ ST and NST occurred in the present study between days 1 and 2, to a maximum level in the period days 2 to 5, which has also been observed in other investigations (Reid et al. 1974, Madias et al. 1975, Merx et al. 1977, Hardarson et al. 1978, Essen et al. 1979a, Inoue et al. 1979, Zmyslinski et al. 1979). This re-elevation mainly occurred in the same area as the primary ST elevation, as there was a close correlation between the primary and secondary ST elevations. It is of interest to note that in standard ECG recordings a secondary rise of ST elevation has also been observed in both anterior and inferior AMI (Thayssen et al. 1975).

There is no general agreement as to the cause of this re-elevation, but a number of theories have been suggested (IV). The possibility of infarct extension or expansion is particularly enticing. Some authors have pointed out that due to a secondary increase in CK concentration in serum with, at times, new clinical events, there is a real possibility that an extension of the myocardial necrosis is the explanation of this secondary rise in ST elevation (Reid et al. 1974, Essen et al. 1979a, Fraker et al. 1979). On the other hand, clinico-pathological and echocardiographic studies have indicated that expansion of the infarction (dilatation and thinning of the infarction area) is a more probable explanation

of the ST re-elevation (Hutchins and Bulkley 1978, Eaton et al. 1979).

From the present clinical results, it is difficult to determine whether an extension, expansion or both are applicable. It would appear reasonable to assume that infarct extension is present when the ST re-elevation is accompanied by re-appearance of CK in plasma and/or additional alteration of the QRS complex, while infarct expansion is presumed to occur when ST re-elevation takes place alone. Defined in this manner 9 patients suffered from infarct expansion, while 5 had infarct extension (IV). Further, it has been reported that infarct expansion produces a deterioration of left ventricular function (Hutchins and Bulkley 1978, Eaton et al. 1979). This may have contributed to the many cases of cardiac failure in this study.

There is general agreement that the development of the Q wave commences early after the onset of anterior infarction, i.e. within 2-3 hours (Rubenstein and Freitas 1978, Selwyn et al. 1978a,c, Fox et al. 1979). On the other hand, there is little agreement as to when Q waves are completely developed, some find within 12-24 hours (Selwyn et al. 1978a,c, Yusuf et al. 1978, Essen et al. 1979b, 1980, Fox et al. 1979), while other authors have demonstrated that the Q wave develops within 24-72 hours (Inoue et al. 1977, Rubenstein and Freitas 1978), and the present study reflects this spreading.

Following an acute transmural infarction, the pathologic Q waves may persist unchanged or they may regress in size, in some cases disappearing entirely (Goldberger 1975). In a study where the Q (QS) waves were recognized after the Minnesota code criteria, similar to the present study, it was found that abnormal Q (QS) waves had disappeared within 2 months in 25% and within one year in 32%, respectively, of the patients suffering from anterior AMI (Pyörälä and Kentala 1974). With regard to the amplitude of the Q waves, it was found in anterior AMI that the sum of the Q amplitudes in the six praecordial leads (V_1 - V_6) decreased significantly from discharge to one year later (Gittler et al. 1956), and by using praecordial ECG-mapping it was shown that ΣQ had diminished by about a third at 6 months (Yusuf et al. 1979b). The results in the present study agree with this, where ΣQ amplitude one year after the infarction had fallen to the same level as at 8 hours. The precise mechanism of regression of abnormal Q waves is not known (Kalbfleisch et al. 1968, Yusuf et al. 1979b), but it is assumed that this takes place owing to shrinking of the infarcted myocardium, as the area of the scar tissue is smaller than the originally injured myocardium (Kalbfleisch et al. 1968, Goldberger 1975).

The amplitude of ΣR was already decreasing at 2 hours, which has also been reported by others

(Selwyn et al. 1977b, Rubenstein and Freitas 1978). It has been stated that the loss of R waves was complete within the first 6 hours (Selwyn et al. 1977b), whereas others, including this study, find that the maximum reduction in ΣR takes place on average, within 24 hours, but with considerable individual variation (Rubenstein and Freitas 1978, Yusuf et al. 1978, Essen et al. 1979b, 1980). In cases of anterior AMI when using leads V_1 - V_6 , it has been demonstrated that the sum of the R wave amplitudes increases significantly from discharge to one year (Gittler et al. 1956); using praecordial ECG-mapping, it was seen that ΣR had risen by 74% one year after discharge (Yusuf et al. 1979b). The results in the present study agree, as the amplitudes of ΣR rose from the 2nd week to one year after the onset of infarction.

The feasibility of predicting the changes of the QRS complex from the early ST elevation has attracted much interest. In patients with anterior infarctions, maximum ΣST has been shown to be related to final ΣQ and ΣR , and suggested that this could be used to predict infarct size (Yusuf et al. 1979a). As the actual maximum ST elevation can be difficult to determine in the individual patient without multiple ECG recordings, the majority of clinical investigators prefer to predict the development at a preset time, e.g. from the ST elevation 2-3 hours after the onset of infarction (Selwyn

et al. 1978a,c, Fox et al. 1979), or after 4 hours as in the present study (ST_{prim}).

Only weak correlations were found between ΣST_{prim} and the development of ΣQ and ΣR within 24 hours of the onset of the infarction. Similar to this, others have found no relation between ΣQ at 24 hours and ΣST at 6 hours (Selwyn et al. 1978a), but in the latter study a close correlation was observed between ΣQ at 24 hours and ΣST at 45 minutes after the onset of chest pain ($r = 0.87$). This would suggest a better prediction following measurement of ΣST very early.

Good correlations have been demonstrated between the number of praecordial positions showing pathological Q waves in a map at 24 hours and the number showing ST elevation (NST) at 2-3 hours ($r = 0.91$), at 4-6 hours ($r = 0.92$) and at 12 hours ($r = 0.92$), after the onset of chest pain (Selwyn et al. 1978c). Such a constant correlation is somewhat surprising when the fact is taken into consideration that the ST segment, as earlier mentioned, is subject to considerable change during this period. This would indicate that NST is insensitive for detecting ischaemic changes and thus the variability of NST is small.

On the other hand a pronounced variability has been observed in ΣST , ΣQ and ΣR , and this may be of vital importance with regard to the poor prediction in the present study, as it has recently been pointed out

that the less precise relationship between these ECG signals can be caused by great between-variability (Selwyn et al. 1978d). In an attempt to avoid the influence of this inter-individual variation, correlations in the present investigation were also carried out between ST elevation at 4 hours and the development of Q and R waves in each lead of the maps of each individual patient, but only a weak or no correlation at all was found. These findings are in agreement with another investigation, where it was impossible to show any meaningful correlation between initial ST segment measurements and subsequent changes in Q and R waves in corresponding leads (Zmyslinski et al. 1979). A great inter-lead variation is the possible explanation of this weak relationship. A considerable inter-individual variation and inter-lead variation are also the most likely explanation of the absence of any correlation between the size of the infarction determined by enzyme analysis and the development of QR waves in ECG-maps. Consequently, in the present study QR changes within 24 hours could not be used for the estimation of infarct size. However, others have shown that the changes of Q and R waves within 24 hours are correlated with the infarct size expressed by the total MB CK activity released into the plasma (Selwyn et al. 1977b).

In this context, it should be noted that no correlation could be demonstrated between $CK-AF_{cum}$ and ΣST at 4 hours, thus making the use of ΣST at 4 hours somewhat questionable with regard to predicting the final infarct size.

The poor prediction of the development of QR waves as well as infarct size may reflect the fact

that all areas with ST segment elevation are not destined to follow the same course. It is possible that some of these regions reflect myocardium undergoing necrosis, some on the way to recovery, and other areas show ST segment elevation as a result of transient ischaemia due to coronary spasm (Oliva et al. 1977, Madias 1979). Finally, it should be borne in mind that infarct extension will complicate any comparison between early ST elevation and ultimate QR changes (IV). Other investigators have found a better prediction by looking at the ST elevation very early, e.g. at 45 minutes after onset of infarction (Selwyn et al. 1978a), but this improvement in the prediction has an obvious disadvantage; very few patients are admitted to hospital so early after the onset of symptoms.

The correlation between ST elevation and clinical variables.

In the 16 patients with anterior AMI, the measured values of Σ ST and NST within the period 4 hours to 14 days were related to the clinical variables measured simultaneously, i.e. heart rate, blood pressure and respiratory rate (III).

It was demonstrated that the heart rate was correlated to Σ ST ($\bar{r} = 0.61$, $P < 0.001$), and NST ($\bar{r} = 0.65$, $P < 0.001$) (Table IX), whereas there was no relevant clinical correlation between Σ ST and NST, respectively, and the mean arterial blood pressure, the

product of heart rate and systolic blood pressure, and respiratory rate (III).

Comments

A complex relationship between ST elevation and a number of clinical factors in connection with AMI has been reported (Hardarson et al. 1978) and the same has been observed in the present study. The only correlation of clinical value was that between ST elevation and heart rate.

Table IX. Correlation between the heart rate and Σ ST and NST, respectively, in various numbers of leads of the ECG-maps (16 patients suffering from anterior AMI).

No. of leads	Σ ST		NST	
	$\bar{r}$	χ^2	$\bar{r}$	χ^2
42	0.61	30.41	0.65	11.10
36	0.59	34.77	0.64	11.82
35	0.59	32.53	0.62	9.14
24	0.58	31.29	0.59	11.73
6	0.60	33.97	0.54	8.94
1	0.40	32.64		

Evaluation of the number of leads employed.

An attempt was made to determine whether a correlation was also present between heart rate and ST elevation, when less than 42 leads were employed in

the ECG-map (Table IX). Various motives were applicable when constructing maps with fewer leads. A map comprising 36 leads was obtained by excluding the 6 leads in row 1 (see Fig. 5) as it has been shown that ST elevation in these leads does not of necessity represent myocardial ischaemia, but may be a normal variant (Edeiken 1954). Thereafter a map containing 35 leads was constructed by the simple process of excluding row F as 35 leads had been used in the pioneer work of Maroko et al. (1972). Following the exclusion of rows A and F there were 24 leads in a map. Finally a map containing 6 leads was made by using positions C1, C2, C3, D4, D6, and D7 (Fig. 5) corresponding to the positions of V_1 , V_2 , V_3 , V_4 , V_5 , and V_6 (Committee of the American Heart Association 1938). The lead with the highest initial ST elevation was used when only one lead was required.

When the heart rate was related to both Σ ST and NST it was found that the mean coefficient of correlation for the number of leads from 6 to 42 did not differ significantly. Whereas there was a significant difference with regard to Σ ST but not to NST between one and 6 leads (Table IX).

As in Chapter III the distributions of the coefficients of correlation were evaluated by means of χ^2 distribution (Snedecor and Cochran 1969, Documenta Geigy 1975). It can be seen from table IX that the χ^2

values for all the selected number of leads were of the same order of magnitude following correlation to ΣST , and of the same magnitude, although less than that for ΣST , with correlation to NST , i.e. the inter-individual variation remained almost constant irrespective of the number of leads.

Table X. ΣQ , NQ and ΣR , NR in each 42-leads ECG-map correlated to the corresponding ECG components in fewer leads of the same map (16 patients suffering from anterior AMI).

No. of leads	Mean coefficient of correlation ($\bar{r}$)			
	ΣQ	NQ	ΣR	NR
35	0.99	0.98	0.99	0.98
24	0.97	0.96	0.99	0.92
6	0.90	0.73	0.95	0.58
1	0.80		0.52	

As shown in table X ΣQ , NQ and ΣR , NR in each 42-leads ECG-map were correlated to the corresponding ECG components in fewer leads of the same ECG-map (35, 24, 6 and 1). The mean coefficients of correlation of ΣQ and ΣR waves in 35 and 24 leads were very high. For ΣQ and ΣR in 6 leads, the $\bar{r}$ values were also very high and both significantly higher than the

corresponding $\bar{r}$ values in one lead. The $\bar{r}$ values of NQ and NR in 6 leads were both low.

Comments

As ECG-mapping with 42 leads is a time-consuming procedure it would be interesting to know whether a map with fewer leads gives valid results. It was found, by relating heart rate to Σ ST and NST, that it was of little importance whether 6 to 42 leads were employed. Further, the inter-individual variation remained of the same magnitude irrespective of the number of leads, i.e. the number will have no effect on the number of patients necessary in clinical trials.

The use of a single carefully selected praecordial lead has been proposed as a practical simplification of the praecordial mapping technique; good correlation has been reported in experiments between Σ ST in an 18 lead map and ST elevation in a single lead, placed at the point of maximum ST elevation (Capone and Most 1979). In the present clinical studies the single praecordial lead was selected from the site, which initially showed the highest ST elevation. In Chapter III it was mentioned that measurement in such a lead produced extremely dispersed coefficients of correlation between heart rate and ST elevation. However, the measurements in this investigation were not commenced at the same time after the onset of the infarction (I), but when carried

out, as in present study, this dispersion was greatly reduced. On the other hand, the correlation between heart rate and Σ ST (6-42 leads) and NST (24-42 leads) were significantly better than that of one lead. Finally, it was demonstrated that Σ Q and Σ R, on the whole, gave the same information in 42 to 6 leads, and NR in 42 to 24 leads. On the other hand, the use of NQ and NR in 6 leads or Q and R amplitude in one lead were unsatisfactory alternatives.

In general these results indicate: 1) measurement of ST elevation and clinical variables should be carried out according to a set time schedule in order to reduce the inter-individual variation; 2) when using ECG-maps with multiple leads, it appears that the number of leads is of little importance (at least the same information is obtained from 24 to 42 leads); 3) the Σ ST, Σ Q and Σ R in the standard 6 praecordial leads offer a practical alternative to ECG-mapping with a larger number of leads, which has also been reported in another study (Zmyslinski et al. 1979); 4) the use of a single praecordial lead or NST, NQ and NR in the standard 6 praecordial leads gives inadequate information regarding events in anterior infarction.

The application and limitation of ECG-mapping.

The ECG-mapping technique described in this study was a semi-automatic system. The actual

recording was relatively simple causing little or no inconvenience to the patient, but even so the whole measuring procedure was time-consuming. A similar ECG-recording system has been devised by others (Essen et al. 1977, Merx et al. 1977), however, all such systems have the disadvantage that the data sampling is intermittent. A continuous recording technique has been constructed (Luxton et al. 1977), but the validity has not yet been fully proven.

This study has demonstrated, that for monitoring an anterior infarction, ΣST and ΣQ were adequate as there was a good signal to noise ratio of these. However, this was only the case for ΣR within a limited period (6-24 hours).

This investigation has also shown that serial ECG-mapping is useful for detecting new events in the infarct process, however, clinical and other parametres must be employed together with the ECG in order to determine the type of changes taking place.

As mentioned in Chapter III, a serious disadvantage of ECG-technique in cases of infarction is that it is not applicable when non-ischaemic factors influence the ST segment and QRS complex. Further, it cannot be used in cases where a previous infarction gives rise to significant changes in the ST segment and QRS complex.

As the surface ECG results from a balance of diversely oriented electromotive forces (Abildskov and Klein 1962) a posterior extension of an anterior infarction will produce reciprocal changes in the electrocardiographic components recorded in anterior leads. This can be overcome by restricting the use of ECG-mapping to cases where the boundaries of the ischaemic injury can be encompassed. Thus, patients with concomittant acute anterior and posterior wall infarction should be excluded (Muller et al. 1978). The map employed, which in general corresponds to the length of the sternum, reaches from the right edge of the sternum to the left midaxillary line. In cases of anterior infarction this ECG-map will normally completely cover the area with ECG-changes. In this context it should be mentioned that ST segment depression maps have been found useful in monitoring the reciprocal changes of transmural inferior infarction by some investigators (Reid et al. 1971), although, others have not corroborated their findings (Madias et al. 1975).

Other electrocardiographic methods are, however, being developed. Both the vectorcardiographic method and the body surface isopotential mapping technique are applicable regardless of the anatomic localization of the infarction (McLaughlin et al. 1974, Akiyama et al. 1975, Kronenberg et al. 1976, Sugiyama et al. 1977, Kjekshus 1979), but their practical ability must await further research.

CHAPTER V.General comments regarding infarct sizing by ECG.

When using ECG for infarct sizing it is well to remember that the electrical phenomena taking place in the heart are exceedingly complex and that the body-surface deflection is a remote and generalized manifestation of these phenomena. Therefore, even the most exacting and precise use of the body-surface deflection can give, at best, only a vague and general picture of the electrical properties of the heart (Beckwith 1970). Thus, based on theoretical consideration and experimental evidence (as discussed in Chapter II) praecordial ECG-mapping cannot be used for a direct quantitation of the mass of infarcted myocardium, but is only able to provide a qualitative estimate of the infarct size. For this reason, the demonstration of a difference in the development of the QRS complex between two patient groups in clinical trials cannot be referred to an actual amount of salvaged myocardium, but it may be concluded that an intervention producing a favourable effect on the mapping results is more beneficial than one failing to do so (Muller et al. 1978).

Praecordial ECG-mapping has been found to be useful for monitoring directional changes in acute ischaemic injury and, furthermore, the development of irreversible damage of the anterior wall of the heart; but unfortunately, the changes in the subendocardium and the posterior-inferior wall of the heart are not reflected to any useful extent (Maclean 1979). In addition to being inapplicable when non-ischaemic factors influencing the ECG-signals are present, this investigation has shown that ECG-mapping is of limited utility for infarct sizing when anterior wall infarction is complicated by new alterations in the infarction process. Consequently praecordial ECG-mapping can only be utilized in very selected groups of AMI patients. This diminishing its practical application to infarct patients in general.

Controlled clinical trials designed to evaluate the influence of pharmacological agents on infarct size can be carried out, either following randomized allocation of patients to several groups, or the patients can be used as their own controls. Should the first principle be employed, then the present study has demonstrated that a large number of patients are necessary in each group, requiring in actual practice multi-centre trials. This is due to the pronounced inter-individual variation of the ECG-signals, reflecting a considerable between-variability of the evolution and size of the infarction.

Alternatively, the patient may be used as his own control, which in theory would reduce the number of patients required in clinical investigations. This principle has been employed in two different ways. With the first a control period is employed prior to the application of the intervention under study. Following this the effect of a treatment is evaluated based on the course of the ST segment. However, the validity of this procedure has been criticized due to among other things the spontaneous increase and decrease of the ST segment elevation in the early phase of AMI (Meerbaum and Corday 1977). The second, is based upon the method of prediction. This model in which the ST elevation during the reversible phase has a predictable progression to QRS configurations indicative of irreversible injury is theoretically very attractive, but as this investigation has shown, there are many objections to this method also. Additional study is necessary, and it has recently been suggested that the enzymatic estimated infarct size may be determined from the initial height of the ST elevation and the logarithm of the early rate of R wave decline (Henning et al. 1978), but whether this approach represents an actual improvement of the electrocardiographic predictive model will require further evaluation.

Investigations of infarct size have made clinicians aware of the dynamic nature of myocardial

infarction in its early stages. The acquisition of this knowledge is in particular due to the electrocardiographic technique, giving an instant insight in the time-sequence of the infarction process. Other non-invasive methods for infarct sizing are unable to provide this momentary picture in the early phase, which gives ECG a distinct advantage.

The semi-automatic mapping system having 42 leads, was both a laborious and time-consuming method. There are two alternatives; one would be to develop a fully automatic system, but this would be expensive in relation to the expected benefit and, in addition, require frequent repeated checking of the ECG-analysis. The other would be to simplify the system. In this respect, the present study has shown that in cases of anterior AMI the number of leads can be reduced from 42 to the six standard praecordial leads without substantial loss of information, and in cases of inferior AMI the lead aVF can be used for monitoring the infarct development. Thus, the employment of standard ECG equipment provides reliable parameters for a qualitative evaluation of infarct size.

SUMMARYChapter I.

The size of an acute myocardial infarction influences the development of pump failure, the severity of which is related to the occurrence of congestive heart failure or cardiogenic shock. Several characteristic stages of cell injury occur during the development of an infarction. This injury is initially reversible but later becomes irreversible unless favourable metabolic or physiologic events improve the oxygen balance in the threatened area of the myocardium. The term infarct size refers to the extent of irreversible myocardial cell damage.

The estimation of infarct size in vivo in clinical investigations requires non-invasive methods, where research has been concentrated on electrocardiography, enzyme analysis, radionuclide imaging and echocardiography.

Characteristic changes of the ST segment and the QRS complex occur during the progression of myocardial infarction. Analysis of these ECG-changes together with the use of multiple leads (ECG-mapping) in experimental studies have created the basis for assessing the extent of the infarction. The object of the present investigation has been to study the usefulness of praecordial ECG-mapping in the clinical evaluation of infarct size.

Chapter II.

The electrophysiological basis of ST elevation is not fully clarified, but is presumed to be the result of a compensated TQ segment depression and a "true" ST segment elevation. The TQ depression is a consequence of changed ion transport across the cell membrane within the ischaemic area. In experimental studies, ST elevation has been correlated to a number of factors, such as myocardial-blood supply, metabolism, enzyme depletion, as well as ultrastructural changes, but a precise quantitative relationship has not been observed. On the other hand ST elevation gives qualitative information regarding the ischaemic changes in the myocardium.

Several theories have been proposed regarding the QRS changes following infarction. According to the cavity potential theory, the occurrence of Q waves is the result of transmission of negative cavity potentials through the electrically inactive tissue to the above lying electrode, while inactivation of the outer ventricular layer is primarily responsible for the reduction in R wave amplitude. The vector theory states that QRS changes are a result of changes in the balance between positive and negative electromotive forces in the heart. Thus, a Q wave can be the result of a loss of positive forces, as can be seen with an infarction and other non-ischaemic myocardial injury. Experimentally a good correlation has been found between QRS changes and necrosis of the myocardium. However, a precise quantitative

relationship cannot be expected as an infarction must be of a certain volume before it is registered as a Q wave in the epicardium or praecordium.

Chapter III.

The first part of the project was planned so that the ST elevation-and the QR amplitudes were measured hourly via a single lead from the body surface on 30 AMI patients for 48 hours after the onset of symptoms, and on 25 control patients for 24 hours. In patients with anterior AMI, the measurements were made via the praecordial lead which initially showed the highest ST elevation (selected from 42 praecordial sites), while V_3 was used in control patients. aVF was employed in patients with inferior AMI as well as in control patients. The ECG-components were analyzed by means of an electric measuring table connected to a desk-computer. The reliability of the measurements was good, as the errors-of-measurement were 4-7% (coefficients of variation).

There was a significant inter-individual variation of the ECG-components in both patient groups. In aVF the intra-individual variation was significantly greater in the infarction group than in the control group, i.e. there was a good infarction signal to background noise ratio in this lead. In the selected praecordial lead, this signal to noise ratio was also good with regard to ST elevation, but unsatisfactory in respect of the R wave.

In the patients with inferior AMI the ST

segment became elevated, on average, to a maximum at 2-4 hours after the onset of infarction; afterwards the ST elevation decreased to a uniform level between 12-48 hours. The Q and R waves began to increase respectively decrease within 4 hours. The development of the QR amplitudes was progressive within 12-16 hours, after which there were only slight changes. The complete development of the QR was considered as the difference between the respective amplitudes at the 2-4 hour and 23-25 hour intervals (ΔQ and ΔR , respectively). $\Delta(Q+R)$ was reasonably well correlated to the enzymatically estimated infarct size. On the other hand the correlation between ST elevation at 2-4 hour and $\Delta(Q+R)$ and the enzymatically determined infarct size, respectively, were relatively weak.

In the AMI patients, the ST elevation was correlated to clinical parameters such as heart rate, blood pressure, respiratory rate, oxygen treatment and the occurrence of chest pain, but the correlation pattern differed considerably.

ECG recording via a single lead is a simple non-invasive technique. The use of aVF is appropriate for monitoring the development of an inferior infarction. In contrast, the use of the precordial lead, which initially had the highest ST elevation, is not advisable for following the development of an anterior infarction.

Chapter IV.

In the second part of the project precordial

ECG-mapping (42 leads) was carried out on 16 patients with anterior AMI and on 10 control patients. The mappings were performed according to a set time schedule during the acute phase and furthermore one year after the infarction. ΣQ , ΣR and ΣST were calculated for each ECG-map; NST only in the AMI group. The reliability of the measurements was good, inasmuch as the errors-of-measurement gave coefficients of variation of 2-5%.

There was a pronounced inter-individual variation of the ECG-components in both patients groups. Likewise, there was a considerable time variation of ΣST , ΣQ and ΣR in the AMI group, but only with regard to ΣST in the control group. The infarction signal to background noise ratio was good for both ΣST and ΣQ from 4 hours to 14 days, but in respect of ΣR this ratio was only satisfactory within the period 6-24 hours.

In patients with anterior AMI the primary ΣST elevation was decreasing from 2 to 8 hours. A secondary elevation occurred between days 1 and 2 to a maximum between days 2 and 5, and possibly results from infarct extension or expansion. The course of NST corresponds to that of ΣST . The ΣQ and ΣR amplitudes began to develop within 2-3 hours after the onset of the infarction, and the maximum rate of development occurred within 24 hours. One year later, both ΣQ and ΣR had the same level as that at 8 hours. The prediction of the development of the QR waves within 24 hours from the ST elevation at 4 hours was poor. There was

no correlation between the enzymatically determined infarct size and the development of the QR waves within 24 hours, and for this reason neither $\Delta\Sigma Q$, $\Delta\Sigma R$ or $\Delta\Sigma(Q+R)$ were useful as electrocardiographic estimates of infarct size in this investigation.

There was a significant correlation between the ST elevation (ΣST and NST) and heart rate, whereas there was no clinically relevant correlation between the ST elevation and blood pressure or respiratory rate.

The number of leads in an ECG-map is of little importance, at least the same information is obtained from 24-42 leads. The standard 6 praecordial leads offer a practical alternative to ECG-mapping with a large number of leads. On the other hand, a single praecordial lead provided inadequate information regarding the evolution of an anterior infarction.

The described ECG-mapping system caused no inconvenience to the patient, but was time-consuming. Praecordial ECG-mapping is useful for monitoring the development of an anterior infarction, but cannot be employed in other infarct localizations.

Chapter V.

It may be concluded, based on theoretical considerations and experimental as well as clinical investigations that surface ECG cannot be used for direct quantitation of the mass of infarcted myocardium, but is

only able to provide a qualitative estimate of the infarct size.

Praecordial ECG-mapping has been found to be useful for monitoring directional changes in acute ischaemic injury, but unfortunately is only applicable in cases of anterior infarction, and then only in those patients where the ECG signals are not affected by non-ischaemic factors. As a consequence, praecordial ECG-mapping can only be utilized in very selected groups of infarction patients.

The ECG method has the advantage over other methods for infarct sizing, that it gives an instant insight in the time-sequence of the infarction process in its early stages. In cases of anterior AMI, ECG-mapping with multiple leads can be replaced by the 6 standard praecordial leads without substantial loss of information, and in cases of inferior AMI, the lead aVF may be used for monitoring the infarct development. Thus, the employment of standard ECG-equipment provides reliable parametres for a qualitative evaluation of infarct size.

RESUMEKapitel I.

Størrelsen af det akutte myokardieinfarkt har indflydelse på udvikling af pumpesvigt, hvis sværhedsgrad er relateret til optræden af kongestiv hjerteinsufficiens eller kardiogent shock. Infarktudviklingen er en dynamisk proces, som gennemløber flere karakteristiske stadier af cellebeskadigelse. Denne er initialt reversibel, men bliver senere irreversibel medmindre gunstige metaboliske eller fysiologiske begivenheder forbedrer oxygenbalancen i det truede område i myokardiet. Ved ordet infarktstørrelse forstås omfanget af irreversibel myokardiecellebeskadigelse.

Bedømmelse af infarktstørrelse in vivo i kliniske undersøgelser kræver non-invasive metoder, hvor forskningen har været rettet imod elektrokardiografi, enzymanalyser, myokardieskintigrafi og ekkokardiografi.

Karakteristiske ændringer af ST segmentet og QRS komplekset optræder under infarktudviklingen. Ved analyse af disse EKG-ændringer samt anvendelse af multiple afledninger (EKG-mapping) er der i eksperimentelle undersøgelser skabt grundlag for en vurdering af infarktets omfang. Formålet med den foreliggende undersøgelse har været at undersøge, om prækordial EKG-mapping er en anvendelig metode til klinisk bedømmelse af infarktstørrelsen.

Kapitel II.

Det elektrofysiologiske grundlag for ST elevationen, er ikke blevet fuldstændigt klarlagt, men antages at være resultatet af en kompenseret TQ segment depression og en "sand" ST segment elevation. TQ depressionen skyldes en ændret iontransport over cellemembranerne i det iskæmiske område. I eksperimentelle undersøgelser er ST elevationen blevet korreleret til en række myokardiefaktorer som gennemblødningen, metabolismen, enzymdepletionen samt ultrastrukturelle forandringer, men et præcist kvantitativt sammenhæng er ikke blevet fundet. Derimod giver ST elevationen mere kvalitative oplysninger om iskæmiændringer i myokardiet.

Infarktbetingede QRS forandringer er blevet forklaret ud fra flere teorier. Ifølge kavitetspotentiale teorien er optræden af Q takker et resultat af transmission af negativt kavitetspotentiale igennem elektrisk inaktivt væv til en overliggende elektrode, mens inaktivering af de ydre ventrikellag primært er ansvarlige for formindskelse af R takken. Ifølge vektorteorien er QRS ændringer et resultat af balanceændringer mellem positive og negative elektromotoriske kræfter i hjertet. Således kan en Q tak være forårsaget af tab af positive kræfter, som det ses ved infarkt og andre ikke-iskæmiske myokardieskader. Eksperimentelt er der fundet en god korrelation mellem QRS ændringer og nekroseforandringer i myokardiet. Et præcist kvantitativt sammenhæng kan dog ikke forventes, idet et infarkt

skal have en vis størrelse førend det registreres som en Q tak i epikardiet eller prækordiet.

Kapitel III

I projektets første del blev ST elevationen og QR amplituderne målt time for time via en enkelt afledning fra legemsoverfladen hos 30 AMI-patienter i 48 timer efter symptomdebut, og hos 25 kontrolpatienter i 24 timer. Hos patienter med anteriort AMI blev målingerne foretaget gennem den prækordiale afledning, som initialt havde den højeste ST elevation (udvalgt blandt 42 prækordiale punkter), mens V_3 blev anvendt hos deres kontrolpatienter. Hos patienter med inferiort AMI og hos deres kontrolpatienter blev aVF anvendt. EKG-komponenterne blev analyseret ved hjælp af et elektrisk målebord tilkoblet en bordcomputer. Pålideligheden af målingerne var god, idet metodemålefejlene var fra 4-7% (variationskoefficienter).

Der var en signifikant interindividuel variation af EKG-komponenterne i begge patientgrupper. I aVF var den intraindividuelle variation af EKG-komponenterne signifikant større i infarktgruppen end i kontrolgruppen, dvs et godt infarktsignal - baggrundsstøj forhold i denne afledning. I den valgte prækordiale afledning var dette signal-støj forhold ligeledes godt for ST elevationen, men utilfredsstillende for R takkens vedkommende.

Hos patienter med inferiort AMI eleveredes ST segmentet i gennemsnit til et maksimum inden for 2-4

timer for derefter at aftage til et ensartet niveau inden for 12-48 timer efter infarktets begyndelse. Q og R amplituderne begyndte at tiltage respektive aftage inden for 4 timer efter infarktets start. For både Q og R takker var denne amplitudeudvikling progressiv inden for 12-16 timer, hvorefter ændringerne var små. Den komplette udvikling af QR amplituderne blev anslået som differensen mellem de respektive amplituder i 2-4 timers og 23-25 timers intervallet (ΔQ respektive ΔR). $\Delta(Q+R)$ var rimeligt godt korreleret til den enzymatiske estimerede infarktstørrelse. Derimod var korrelationen mellem ST elevationen i 2-4 timers intervallet og henholdsvis $\Delta(Q+R)$ og den enzybestemte infarktstørrelse relativt svag.

Hos AMI-patienterne blev ST elevationen korreleret til kliniske parametre som hjertefrekvensen, blodtrykket, respirationsfrekvensen, oxygenbehandlingen og forekomsten af brystmerter, men korrelationsmønstret var meget uensartet.

EKG-optagelser via en enkelt afledning er en simpel non-invasiv teknik. Afledning aVF er ideel til monitorering af udviklingen af et inferiort infarkt. Derimod er anvendelse af den prækordiale afledning, som initialt har den højeste ST elevation, ikke anbefalelsesværdig, når det drejer sig om at følge udviklingen af et anterior infarkt.

Kapitel IV.

I projektets anden del blev prækordial EKG-

mapping (42 afledninger) udført på 16 patienter med anterior AMI samt på 10 kontrolpatienter. EKG-mapping blev foretaget efter et fast tidsskema i den akutte fase samt 1 år efter infarktets begyndelse. For hver EKG-map blev ΣQ , ΣR og ΣST beregnet; NST kun i AMI-gruppen. Pålideligheden ved måling af ΣST , ΣQ og ΣR var god, idet metodemålefejlene gav variationskoefficienter på 2-5%.

Der var en udtalt interindividuel variation af EKG-komponenterne i begge patientgrupper. Ligeledes var der en betydelig tidsmæssig variation af ΣST , ΣQ og ΣR i AMI-gruppen, men kun for ΣST i kontrolgruppen. Infarktsignalsbaggrundsstøj forholdet var god for både ΣST og ΣQ inden for 4 timer til 14 dage efter infarktets begyndelse, men for ΣR var dette forhold kun tilfredsstillende inden for 6-24 timer.

Hos patienterne med anterior AMI var den primære ΣST elevation aftagende 2 til 8 timer efter infarktets begyndelse. En sekundær elevation af ΣST , som indtrådte mellem 1. og 2. døgn til et maksimum mellem 2.-5. døgn, skyldtes muligvis infarkt extension og/eller expansion. Forløbet af NST svarede til ΣST . Amplituderne af ΣQ og ΣR begyndte at tiltage respektive aftage inden for 2-3 timer efter infarktets start, og den maksimale udvikling fandt sted inden for 24 timer. Et år senere havde både ΣQ og ΣR samme amplitude som 8 timers niveauet. Prediktionen af QR takkernes udvikling inden for 24 timer ud fra ΣST elevationen 4 timer efter infarktets begyndelse var ringe. Der var ingen korre-

lation mellem den enzymbestemte infarktstørrelse og udviklingen af QR takterne inden for 24 timer, hvorfør hverken $\Delta\Sigma Q$, $\Delta\Sigma R$ eller $\Delta\Sigma(Q+R)$ var anvendelig som elektrokardiografiske mål for infarktets størrelse i denne undersøgelse.

Der var en signifikant korrelation mellem ST elevation (ΣST og NST) og hjertefrekvensen; derimod var der ingen klinisk relevant korrelation mellem ST elevationen og henholdsvis blodtrykket eller respirationsfrekvensen.

Ved EKG-mapping er antallet af afledninger uden større betydning, idet den samme information opnåes fra 24 til 42 afledninger. Samtidig kunne det vises, at de 6 standard prækordialafledninger var et praktisk alternativ til EKG-mapping med et større antal afledninger. Derimod gav en enkelt prækordial afledning inadækvate oplysninger om begivenhederne i et anterior infarkt.

Det beskrevne EKG-mapping system kunne anvendes uden ubehag for patienterne, men var ret tidskrævende. Prækordial EKG-mapping kan anvendes til monitorering af udviklingen af et anterior infarkt, men er ikke anvendelig ved andre infarktlokalisationer.

Kapitel V.

På grundlag af teoretiske overvejelser samt eksperimentelle og kliniske undersøgelser kan det fastslås, at EKG ikke kan anvendes til en direkte kvantitativ måling af infarktets størrelse, men kun til en kvalitativ bedømmelse af denne.

Prækordial EKG-mapping har vist sig at være nyttig til monitorering af ændringer i den akutte iskæmiske beskadigelse, men uheldigvis kan metoden kun anvendes til anteriore infarkter og kun i de tilfælde, hvor EKG-komponenterne ikke er påvirket af non-iskæmiske faktorer. Den praktiske anvendelighed af prækordial EKG-mapping er derfor begrænset til selekterede infarktpatienter.

Fremfor andre non-invasive metoder til bedømmelse af infarktstørrelsen har EKG-metoden den fordel, at den giver hurtig indblik i infarktprocessens udvikling i den tidlige fase. I tilfælde af anteriort AMI kan EKG-mapping med multiple afledninger uden væsentlig tab af information erstattes af de 6 standard prækordialafledninger, mens afledning aVF foreslåes anvendt ved inferiort AMI. Standard EKG-udstyr er således i stand til at give pålidelige parametre til en kvalitativ vurdering af infarktstørrelsen.

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